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MEDICINE IN THE NATIONAL DEFENSE PROGRAM

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SINCE THE MEMBERS of the Southern Surgical Association are all members of the American Medical Association, I felt that you would be interested in knowing of the work of its Committee on Military Preparedness. This Committee was appointed at the session of the House of Delegates in New York in June, following a request of the Surgeons-General of the Army, Navy, and Public Health Service that the American Medical Association undertake a survey of the profession in the United States regarding the qualifications and availability of its members for service.

There are 179,000 doctors entitled to practice in the United States by means of legal registration, and a questionnaire was sent to each of these. Between 140,000 and 145,000 are in active practice, while the remainder have retired because of age, disability, or having sought other pursuits. So far, 125,000 replies have been received, of which over 75,000 have been transferred to punch-cards. These punch-cards contain the information furnished by the questionnaires, and by using them in the International machine, one may in a few minutes get a list of qualified men in any given branch of medicine. This work has been undertaken by the American Medical Association as a patriotic contribution to the National Defense Program, and has entailed the employment of an additional 16 persons in the American Medical Association's office. It is hoped that within two or three months information will be at hand upon every doctor in the country. The only exemption in the Selective Service Act applies to students of theology and accredited ministers of the gospel. Deferments will be made to students in accredited schools, pursuing a course of study leading to a degree in Arts and Sciences, and, also, to those who occupy essential positions in their community. In order to effectively safeguard the health of the population and to furnish medical service to the armed forces, the medical profession feels very strongly that medical students should be permitted to finish their undergraduate education and, at least, one year of internship before being inducted into service. The Selective Service Act, however, provides deferment for students only until June, 1941; after that date any deferment granted

to medical students, to interns, and to residents, will be the responsibility of the local Draft Boards. While doctors should be willing to make such adjustments as may be needed in the event of an emergency, it would be unfortunate if in the Defense Program the classes of medical schools, the teaching program of medical schools, and hospital service should be disrupted by an undue number of students, interns, and residents being called into service. This can be avoided only by applying to the local Draft Boards and to the Appeal Boards for the deferment of those essential to these three activities. There are approximately 15,000 members of the Medical Reserve Corps, and these will be largely drawn upon to furnish medical service for the first increment of selectees. It is estimated that by July, 1941, the total strength of the army will be approximately 1,400,000 men, for which the services of 10,000 doctors will be required. The length of service of the vast majority of doctors will be one year, at the end of which time they will be transferred to the Reserve Corps on an inactive status. The information being gathered by the Military Preparedness Committee of the American Medical Association will make it possible to employ the services of doctors in positions for which their training and qualifications fit them, and thus to avoid some of the mistakes and misfits which occurred in the First World War.

The major objectives of the survey are to provide medical service for the armed forces, to provide medical service for industrial mobilization, and to provide continuing medical service for the civilian population. In the First World War more than 32,000 physicians voluntarily served with the armed forces. In the event of war coming to our country again, the profession will similarly give of its members a sufficient number to meet the needs of the Army, Navy, and Public Health Service. Furnishing medical service to the rapidly expanding industrial plants presents many difficulties; it will be no task to supply doctors who are fully competent to care for industrial injuries, but it is quite another problem to supply doctors familiar with the toxicologic problems of industry. Practically all of the metals, many of the solvents, such as benzol and tuluol, and many chemicals used in industry are capable of producing rather disastrous toxic effects upon the human organism. To effectually control these hazards requires the cooperation of the physician who is familiar with the problems and the safety engineer who understands methods of prevention. Continuing the service to the civilian population through hospitals and through men in various fields of practice is essential if the health and welfare of the civilian population is to be protected.

On September 19, 1940, President Roosevelt appointed a Health and Medical Committee, a subcommittee of the National Defense Council; its members are Surgeon-General McGee of the Army, Surgeon-General McIntyre of the Navy, Surgeon-General Parran of the United States Public Health Service, Dr. Lewis Reed, Chairman of the Medical Division of the National Research Council, and your humble servant, representing the

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civilian profession. The duties of this Committee are to advise the National Defense Council on health and medical matters affecting National Defense and to coordinate all health and medical efforts. • The Medical Division of the National Research Council has at present 38 committees, each studying some problem in its relationship to Military Medicine, such for instance as shock, chemotherapeutic treatment of wounds, blood transfusions, aviation medicine, tuberculosis, neuropsychiatry, nutrition, *etc.* The Health and Medical Committee has appointed subcommittees on dentistry, medical education, hospitals, nursing, industrial health and medicine, and Negro health. An effort has been made to secure the advice and help of those whose qualifications in their respective fields entitle them to serve with advantage to the country.

It gives me much pleasure to gratefully acknowledge the unanimous offer on the part of the profession at large, of the various National and Special Medical Societies, of the hospital groups, in fact, of all agencies relating to health and medicine to cooperate fully and freely in the Defense Program.

This paper was read before the Fifty-third Annual Session of the Southern Surgical Association, Hot Springs, Va., December 10, 11, 12, 1940.



SCIENCE AND HUMAN PROGRESS—IV

Radium and Atoms

DALTON'S Atomic Theory and Mendeleeff's Periodic Law developed the idea that all matter was composed of a limited number of kinds of indivisible building bricks, known to us as the atoms of the elements, out of which all things are constructed. While these concepts were indispensable as stepping stones to a better understanding of the structure of matter, they seemed to close the door to the possibility of anything outside of the material.

The discovery of radium smashed these bricks and transformed them into little constellations with a central nucleus, about which revolved electrons at infinitesimal, but relatively great distances from the nucleus. This opened the door to a better understanding of forces, probably enormously more important to the ultimate destiny of Man than the material benefits which have already so magnificently followed the discovery of radio-activity in all its present applications. The unbelievable results derived directly from the discovery of roentgen rays are too apparent for emphasis.

—A. Cressy Morrison, Transactions of the New York Academy of Sciences, Series II, 2, No. 3, January, 1940.

THE TREATMENT OF FRESH TRAUMATIC WOUNDS

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THE SUCCESSFUL SURGERY of traumatic wounds is far more exacting of judgment, skill, and time than is elective surgery. This is readily understandable because in the case of such wounds the surgeon begins his work with damaged, soiled, and contaminated tissues rather than with healthy, clean, and sterile tissues which he encounters in elective surgery. It is to us totally nonunderstandable that this difficult problem elicits so little real interest on the part of leaders of surgery in this country and is commonly delegated to the younger inexperienced surgeons to deal with hurriedly. This erroneous attitude may, in a large measure, be due to the fact that traumatic wounds are not made by the surgeon (at least they are not supposed to be) and, thus, the responsibility for the result can so easily be blamed upon factors other than the judgment and skill of the surgeon. It is not only easy but a great temptation for a surgeon to ease his conscience by ascribing to God or influences beyond his control his tragic results of treatment of traumatic wounds. The reverse attitude is, of course, the correct one; the fact that the surgeon did not make the wound should be a superchallenge to him to use the greatest judgment and skill which his knowledge affords him; and his poor results should never fail to hurt his pride and teach him something.

We want to pursue this thought a little farther, before going on with our paper, by citing a few glaring examples of what we have been discussing. While the most trivial elective surgical problem is being treated in the main operating room under the most rigid surgical precautions, you will often find far more serious, soiled and contaminated traumatic wounds being treated improperly, under trying and questionable circumstances, in the Out-Patient Clinic. Is there any logic in this when, with the exercise of more care, patience, and skill, under the conditions obtained in the general operating room, such wounds may be made to approach the cleanliness and sterility of the elective case? The answer is unequivocally "no," when the dirty, contaminated wound is on your son or the son of any other doctor who knows not only the importance of but the surgical skill required for rendering the proper toilet and repair of such wounds.

Recognizing the tendency as well as the temptation to extend the services of the accident room to include so-called minor traumatic wounds which we do not at all regard as minor, we have found it advisable to make certain rules regarding the cases which may or may not be treated in the accident

department. For example, no open wounds which may have involved tendons, nerves, bone, important blood vessels, or may have pierced any of the cavities of the body can be treated there. Except for the control of hemorrhage, in the performance of which we decry the use of the tourniquet, and the general treatment of shock, we demand that such wounds be rigidly left alone until the proper type of treatment can be carried out in the main operating room. The wound is simply covered with dry gauze and immobilized until the operating room is ready and the patient is in condition to be taken there. Any half-hearted attempts at the cleansing or sterilization of such wounds in the accident room is strictly forbidden. It is inexcusable to yield to the temptation to pull a protruding end of bone back beneath the skin. In other words, we believe the first chance at the toilet of a traumatic wound is the all-important chance. When a surgeon secures this chance within the period of contamination (six to eight hours), we are not very sparing of our criticisms if he attempts to secure primary healing of the wound and fails.

We have come to believe in, and have adopted, certain fundamental principles regarding the treatment of traumatic wounds. Most of them are very old and the value of many of them was first clearly demonstrated during war-time experiences. It may be well to review briefly those principles:

(1) *Hemostasis or the control of hemorrhage* is certainly the oldest and one of the most fundamental. Its importance was obvious and remains so to-day. It appears to us, now, that for centuries this was about the only worth while principle clearly in the minds of those who treated wounds even though their efforts to practice it were often harmful and inhuman. In the light of our present knowledge, it seems that their efforts to promote wound healing, by ointments and concoctions, could have been of little or any benefit.

(2) *The prevention of, or the elimination of, necrotic tissue, débris, and foreign bodies in wounds* was the next fundamental principle of wound treatment to emerge. It is true that Paracelsus, and others had recognized it but it was Paré, who, over 400 years ago, brought it forcibly to the attention of the medical profession. He stopped many of the efforts to control hemorrhage, which were violating this principle. The importance of this principle was immeasurably strengthened and the technic of observing it vastly improved during the World War (1914-1918). It is now firmly established under the name of "*débridement*."

(3) *The value of rest or immobilization of wounds* was particularly stressed by Baron Larrey in the Napoleonic wars. In recent years, a revival of interest in this principle of therapy has been due largely to Winnett Orr and Koch; its value was unquestionably demonstrated by the Spanish military surgeons, particularly J. Trueta, during their recent civil war. What is not yet as generally recognized or practiced, as it should be, is that immobilization is just as valuable in the treatment of soft tissue wounds as it is in the treatment of wounded bones.

(4) *Efforts to control infection in, or to eliminate contamination from, fresh traumatic wounds does not justify the use of substances which are injuri-*

ous to living cells. This we know is a debatable point, and we state, for what it is worth, our position, which is that we know of no antiseptics which we are willing to put into fresh wounds.

(5) *The preservation of a proper blood supply* to wounds is vitally important and not only from the mere necessity of trying to avoid sloughing. When our conception of this principle is enlarged from the narrow one of the actual amount of blood flowing to the tissues of a wound to include the character and quality of blood supplied to the wound, there arise considerations not dreamed of until within recent years. These involve the use of blood, blood plasma, fluids, electrolytes, vitamins, proteins, etc., all in an effort to restore to the patient and, consequently, to his wound an essentially normal blood which we know to be a great aid to wound healing. Besides, there are relatively simple means of determining the deficiencies of these various substances in the blood. We must know them, we must use them whenever possible; we must learn more accurately to recognize clinically these deficiencies when the laboratory aids are not at our command.

(6) It is essential to have some clear-cut conception of the difference between *bacterial contamination* and *bacterial infection* of a traumatic wound. The former we regard as a surface involvement with very little bacterial proliferation or invasion; the latter as an invasive process with definite bacterial proliferation.

(7) *Fresh wounds, surgical or traumatic, are rarely, if ever, absolutely free of bacteria; their sterilization is relative.*

(8) *Granulation tissue is essential to the healing of all wounds.* In the absence of the body surfaces' normal protection, it is nature's best protection against infection.

(9) *The healing of wounds is brought about by the growth and activity of living cells, save for what is accomplished by contraction.* Some knowledge of tissue culture makes this principle far more valuable and understandable.

(10) *Tetanus and gas bacillus antitoxin* should be used prophylactically whenever the nature of the wound and the severity of its soiling indicate their use. Here it is difficult to make any hard and fast rules. With us, the matter is largely determined by our satisfaction with the thoroughness of the débridement or the toilet of the wound. When we feel justified in an attempt at primary closure of the wound we are less inclined to use either one of them.

(11) More or less as corollaries or amplifications of some of the above principles, it should be stated that *healthy living cells have a remarkable power to combat bacteria*, that *dead or devitalized tissues are powerless against their onslaught*; that prior to the lapse of six to eight hours the bacteria in a fresh wound may be considered as being on the surface of the wound and not invading the living tissue; that the position of a wound may be an important factor in its blood supply; that dressings and the temperature may influence the blood supply and the growth of living cells, etc.

This declaration of faith in certain principles which guide us in the treatment of traumatic wounds is not sufficient, for it is obvious that a slave-like

devotion to some of them cannot help but mean a sacrifice of certain others. For instance, the overzealous devotee of hemostasis can easily violate the principles of débridement. It is, therefore, proper that we should tell you in more detail how we attempt to make use of them.

When the patient is first seen, no attempt is made to do anything to the wound except to control hemorrhage, if this is necessary. We prefer to do this by placing firm pressure on the wound with the hand, through the medium of a sterile dry sponge, while at the same time elevating the part. If there is a rather large active bleeder, this can often be stopped by direct pressure with the point of the finger until a ligature or clamp can be applied to it. Sometimes, mediate pressure with the finger on the main artery away from the wound will accomplish the same thing. We prefer, if possible, never to use the tourniquet simply for the emergency control of hemorrhage, unless upon so badly mangled extremities that they must obviously be amputated. Then, the tourniquet is placed so close to the wound that there will be little or no unnecessary loss of the part when the amputation is done. During the control of the hemorrhage, if there is other available professional help, the degree of shock should be assayed and efforts set in motion to combat it. With these things accomplished or underway, it is time to take "time out" and consider carefully what the next steps should be. The surgeon might ask himself innumerable questions.

What does this patient's condition warrant doing? Is it safe or wise to remove the patient to the hospital, or from the accident room to the operating room, and how shall the wound be immobilized during the process? If serious shock has been combated, will there be similar means of combating it (blood, plasma, fluids, *etc.*) at the destination of his transport and during any operation which might be decided upon there? Is it being borne in mind that, though this patient has at the moment been brought out of shock, he can go back into shock with alarming rapidity during manipulation or operative procedures? If it is assumed that the wound and the patient's condition justify some operative procedure then one should ask himself some other questions. Shall this wound be regarded as contaminated or as infected? Is it a simple incised wound which needs only cleansing and repair? Is it so soiled and traumatized that it should be completely excised (débridement), cleansed, and primarily closed or skin grafted? Are there damaged vital structures such as nerves, tendons, and blood vessels which will prohibit a complete débridement but will permit sufficiently satisfactory cleansing to justify preparations for an attempt at delayed primary suture or grafting? Are the nature of the wound and the circumstances of its occurrence such that only the points of entrances and exit should be treated and the wound immobilized? Is the wound so obviously infected and soiled that it should be treated only with the idea of secondary closure, of later skin grafting on the granulation tissue, or of allowing it to heal spontaneously? After deciding what is ideal, the surgeon must decide what is practical with the facilities at hand and the conditions under which he must work.

With a belief in the fundamental principles of treating fresh traumatic wounds as we have enumerated them, we do not often have any difficulty in answering the above questions so far as the wound is concerned. With facilities for determining the hematocrit reading, the blood proteins, the fluid and electrolyte needs and with blood, blood plasma, and other solution always ready for immediate use, the answer to these questions from the point of view of the patient's status is not nearly so difficult as it used to be.



FIG. 1.—A sponge has been tucked into the wound so as not to overlap the adjacent skin. The area has been shaved and is being washed for ten minutes with soap and water. This will be followed by alcohol and ether skin preparation.

Let us take a few examples to illustrate in more detail just what we do with different types of wounds.

(1) *A simple incised and contaminated wound.* By this we mean a wound of less than eight hours' duration in which there is no discernible damaged or devitalized tissue which requires débridement.

The operator scrubs up and puts on gloves. A dry sponge is placed in the wound so that it will not overlap the edges. The skin in the field of operation is shaved, then thoroughly scrubbed with soap and water for ten minutes up to the edges of the wound, all grease and dirt having been removed with benzine or ether. The skin is now cleansed with alcohol and ether, and then painted with tincture of merthiolate. None of the benzine, alcohol, ether or merthiolate is permitted to enter the wound. Gloves are changed and the wound draped as though for a sterile operation. The wound is then anesthetized with novocain introduced well away from the wound. Following this, the sponge is removed and every recess of the wound carefully inspected for foreign bodies which should be removed. If there is no grease or staining of living tissues which may require the use of soap and water, the wound is carefully washed with normal salt solution, using the gloved finger for gentle rubbing of the raw surfaces. When the cleansing is complete so that all tissues look clean, healthy, and normal, the wound is again copiously irrigated with normal salt solution. The skin is again dried and recoated with merthio-

late. Gloves are again changed and new drappings applied right up to the edges of the wound. The repair of the necessary deep structures and of the skin is made throughout with silk sutures. It should be added that a minimum amount of silk is used for the ligatures of blood vessels and the suturing of fascial planes. Severed tendons and nerves, and occasionally large blood vessels, are accurately approximated with it. After closure of the skin, which may be by primary suture or with the aid of grafts and always without drains,

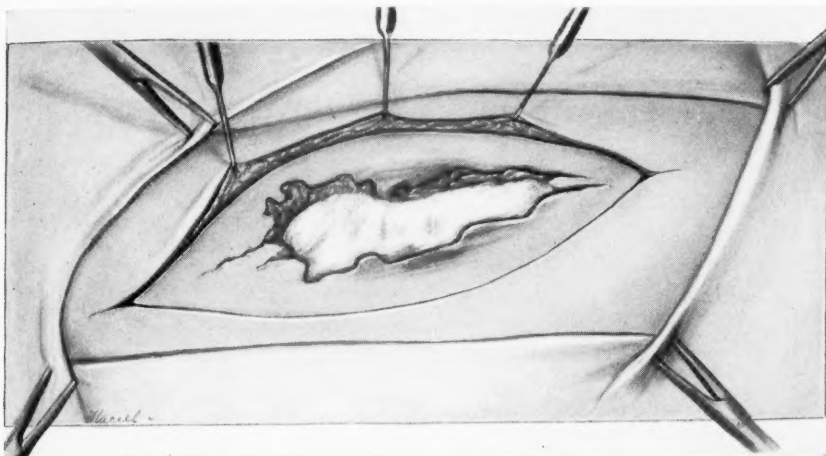


FIG. 2.—The skin has been painted with a skin antiseptic up to the wound edges and draped. No skin antiseptic and no alcohol, ether, or soap has been allowed to enter the wound. The excision of the wound has been started.

the wound is dressed with a moist saline gauze and, if possible, completely immobilized. The wound is not dressed until there is some indication for doing so. This might be at the end of three days or more than three weeks, depending upon the possible harm of movement incident to the dressing. The indications for dressing the wound are pain, unexplained fever, impaired circulation to the part beyond, or the necessity of removing stitches. Blood or serum-stained dressings are no indication that the dressing should be changed.

(2) *Delayed primary closure of an incised wound of such duration that it can no longer be regarded as simply contaminated—one which must be regarded as infected although there is no evidence of active suppuration, inflammation, or the formation of granulation tissue.* In this connection, it should be remembered that such wounds about the head and face may be regarded and treated as only contaminated for a much longer period of time than is the case when they occur in other parts of the body.

When, however, a delayed primary closure is decided upon, the procedure is as follows: The steps are exactly the same as just described above, up to the point of repair of the wound. Instead, it is packed loosely in all its recesses with moist saline gauze which is covered with gutta-percha to keep it moist. It is then immobilized for 24 or even 48 hours. On the removal of the gauze pack, if the wound appears healthy, clean, and uninfamed, it is

repaired as though the delay had not occurred. If it is obviously infected or otherwise unfit for closure, the surgeon's course should be planned toward securing healing with the aid of an open granulating surface.

This delayed primary closure is often a useful procedure when what would otherwise be a primary closure has to be terminated because of the patient's condition.

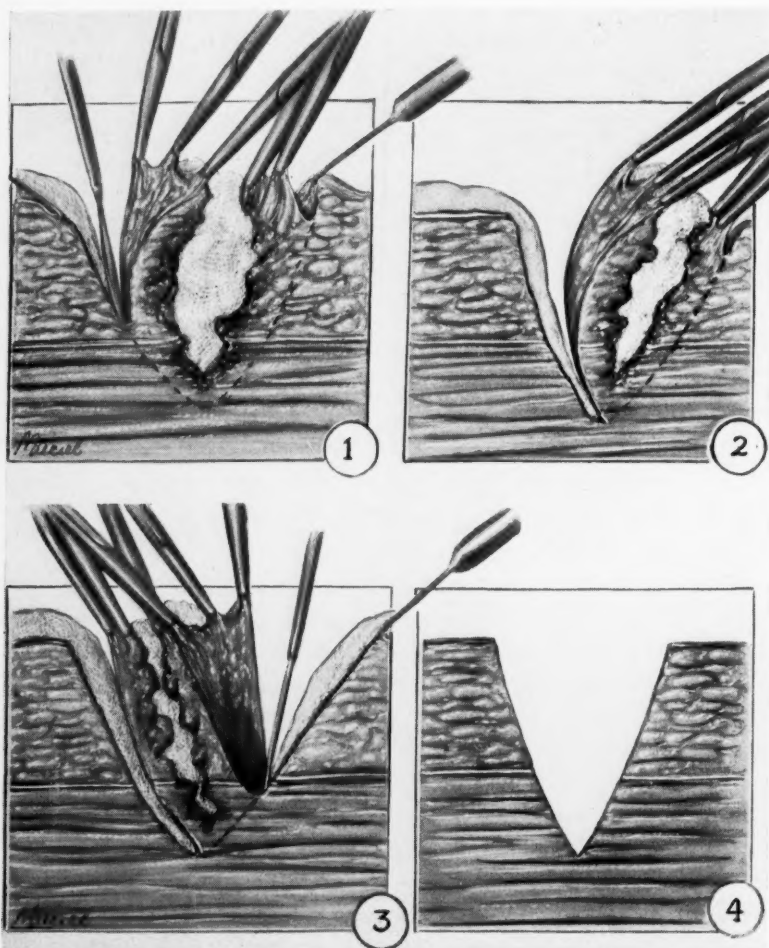


FIG. 3.—(1) Hemostats have been applied to the skin edge which is to be excised. The excision has been carried down to the muscle. Fresh pads moistened with saline have been advanced down the clean side of the wound as the incision is deepened. (2) The excision has been completed on one side. Note the protection by the gauze pad. (3) The excision has been nearly completed. (4) The completed excision. The wound is now irrigated copiously with normal salt solution and fresh drappings are applied.

(3) *Treatment of the superficial point of entrance or the points of entrance and exit of a wound plus immobilization.* Quite often in civil life and to a lessening extent in military life, there will occur stab, rifle or pistol wounds or even fractures, compounded from within, under conditions which warrant local treatment of the puncture wounds only, the remainder of the wound

being undisturbed. We need not elaborate upon this point for we are all aware that the cleanliness of the patient, the type of his clothing, the kind of bullet, the absence of injury to bones, tendons, nerves, *etc.*, are the principle determining factors. As an example, we cite a Chinese war experience in which every bullet or knife entered the body encased in wool carried in from the soldier's uniform. Under such circumstances, it was necessary to lay such

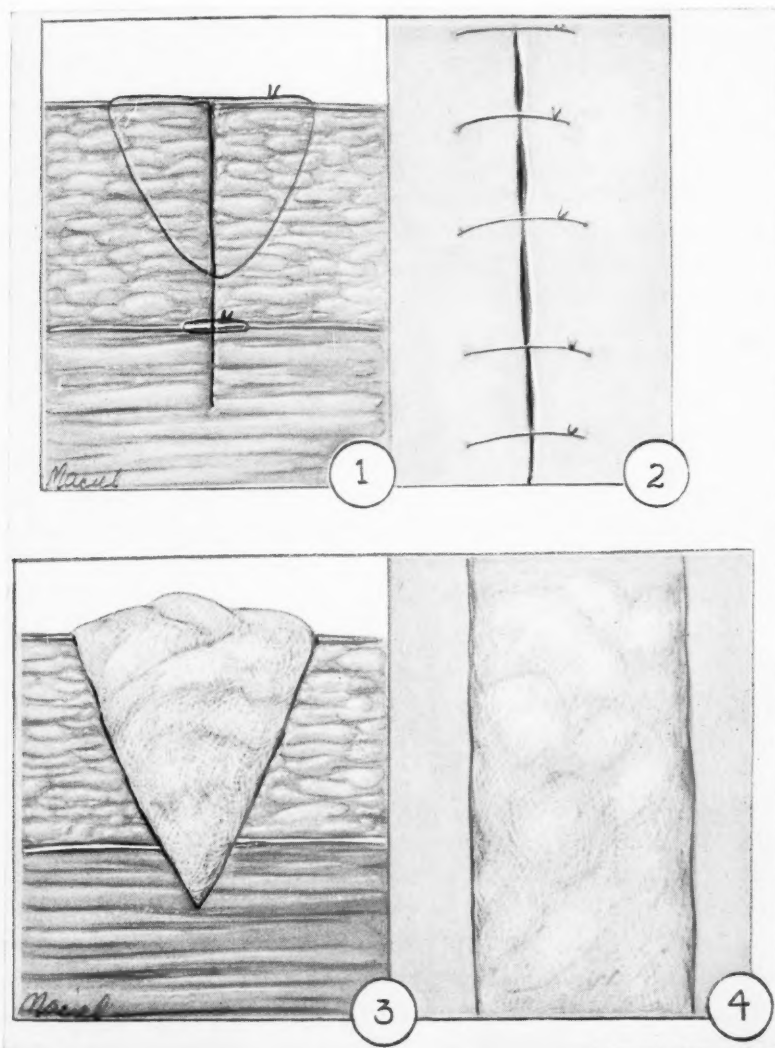


FIG. 4.—(1) and (2): Primary closure of the wound. The fascia over the muscle has been sutured with silk. The skin sutures have been so placed as to leave as little dead space as possible. These sutures are placed rather far apart and tied loosely. (3) and (4): If primary closure is not feasible, the wound is packed loosely with gauze. A plaster encasement is then snugly applied so as to completely immobilize the part.

wounds wide open to the very depth of their extent, to excise the tracks, and to remove all retained foreign bodies, which usually could not be recognized until the wool was removed from them.

When the simpler procedure is adopted, the cleansing of the skin, the draping of the wound, and the introduction of the anesthesia are done as already described. The smooth stab wounds are washed superficially with salt solution and closed without drainage. The gunshot wounds are excised through skin and fat, washed in this area with normal salt solution, as though they were to be closed, and then usually left unsutured. They are filled with vaseline, covered with vaselined gauze and immobilized in a dressing which is not disturbed until there is an indication for doing so.

(4) *The treatment of contaminated, lacerated and obviously traumatized wounds by débridement, cleansing and suture, or suture plus grafting, or grafting alone.*

Such operations are preferably performed under a tourniquet which, because of pain caused by it, usually requires a general anesthetic. When the wound is of a serious nature or on a patient who has been brought out of shock, there is always on hand, in the operating room, intravenous fluids and blood before the operation is begun.

If pain is not a serious factor, the field of operation is prepared, as previously described, before the anesthetic is administered. If the injury is near the hand or foot, the part is scrubbed and the nails given the same meticulous care that the operator would give his own hands.

The purpose of the tourniquet is to save blood and to prevent unnecessary clamping of many bleeding points, which reduces the amount of ligature material in a wound and the time spent to put it there. The tourniquet maintains a clear dry field for the dissection and enables one to avoid soiling of freshly cleansed areas by the overflow of tissue juices and blood, or by frequent sponging of the field with gauze which will so easily touch both clean and dirty areas at the same time and also add unnecessary trauma.

No washing of the wound is done until the débridement is completed for this may not only obscure foreign bodies but will, under the influence of the tourniquet, make it far more difficult to differentiate between living healthy tissue and devitalized tissue which has not yet had time to change its color.

A dry sponge is tucked into the wound. An elliptical incision is made through normal skin about one-quarter inch from the edge in large wounds. This is carefully developed into the fat, but not through it. As the incision approaches the cavity, blood stains are observed in the tissue and its direction is changed. The clean skin flap is undermined as the edge is held up by small retractors. The undermining continues until the subcutaneous fat joins the muscle fascia. If there is doubt as to where this occurs, the clean wound is protected with moist flat gauze, the field protected with towels, the fluff removed from the dirty wound with a clamp and the cavity inspected. Another dry gauze is replaced and the clamp is kept in a separate basin for similar future use. In this manner, the entire wound is followed through the muscle fascia and torn muscle bellies. Long muscle fibers are split with a knife and incisions crossing the fibers are best made with small scissors. Areolar tissue

can be followed along periosteum, vessels, tendons, and nerves. The field and clean wound should always be protected with towels and moist gauze, so that in case of contamination the protection can be changed or removed, rather than covered over and allowed to remain as another source of unrecognized contamination.

Often the dirty wound and all devitalized tissue can literally be lifted out, *en masse*, without a serious break in technic. The wound is then washed with normal salt solution. Gloves and gowns are changed, clean instruments are secured, and the field again redraped up to the edges of the incision, after another coating with tincture of merthiolate which must not enter the wound. Before the tourniquet is removed any known or discoverable open vessels, which are sure to bleed, are ligated with fine black silk. The wound is packed with dry gauze which is held in place, with decreasing firmness, for several minutes after the tourniquet is removed. This will stop many small bleeding vessels and make unnecessary the use of many ligatures which cannot help but add some necrosis to the wound. As this gauze pack is teased out, the other bleeders, obviously requiring ligature, are clamped and tied. Then, the oozing and smaller bleeding points, which one prefers not to tie, can usually be stopped by gentle pressure with warm (not hot) moist gauzes. Any overlooked pieces of ischemic tissue, revealed by the returning circulation, should now be carefully trimmed away. The wound is again washed with normal salt solution and closed throughout with fine silk or, if necessary, grafted. The wound is dressed with a dressing which secures complete immobilization and is not disturbed until all danger of manipulation from removing it is gone. If it is necessary to remove the skin sutures before one is ready to change the encasement this can be done through a window cut in the encasement. As will be noted later in this paper, it is felt very unwise to cut a window in an encasement covering a wound which has been packed with gauze. However, there seems no good reason for not doing so in the case of a wound which has been closed primarily or grafted, provided the window and dressings are replaced with their original degree of firmness.

Severed tendons and nerves, and compound fractures often give the most trouble in carrying out this ideal débridement, cleansing, and closure. In the latter cases, the dirty cavity is entered when the broken fragments are encountered. However, there need not be any contamination if one is careful to keep the clean surfaces covered. The soiled specimen is clipped free and discarded. The wound is next lengthened in either longitudinal direction until the end of either fragment can be brought out for further débridement. Soiled periosteum stripped from the bone must be sacrificed. It is at this state when the delayed washing of a wound is most appreciated. Dirt particles are now visible and there is no guesswork in their removal. With an osteotome, or thin chisel, a shaving of cortex is started from the clean portion and carried to the end of the soiled fragment. It is picked off with a clamp and discarded. The entire dirty area of bone denuded of periosteum is cleanly

shaved in this manner. The tip of the fragment, if dirty, is cut off with the same instrument or perhaps a saw or bone cutter. It is not advisable to use a rongeur for any part of the work. Its biting edges always pass through soiled surfaces, besides tending to leave partially detached pieces of bone.

When débridement of the fragment is completed, it is covered with gauze and returned to the wound. The end of the other fragment is lifted out and similarly treated. After this is done the extreme depths of the wound are systematically given débridement and the cavity is ready for irrigation. Large quantities of warm, but not hot, saline are used. While being irrigated, the wound is gently rubbed with a gloved finger to detach pieces of loose tissue and blood clots.

No mechanical fixation of bone fragments in the wound is employed. Tendons and nerves are sutured with silk. The wound is closed with interrupted sutures of silk. If the closure is under tension, and it usually is in fracture cases, counterincisions are made on either side to give relaxation. These defects may be skin grafted or packed with vaselined gauze and allowed to heal by second intention. Viability of skin over the fracture site depends on a closure without tension; the conversion of a compound fracture to a simple one depends on the skin remaining viable and intact. A moist gauze dressing is applied. The fragments are immobilized by skeletal fixation with pins or by an encasement alone, depending on the type of fracture; but they must be perfectly immobilized. The patient is given the usual prophylactic dose of tetanus and gas bacillus antisera. The dressing is not disturbed for weeks unless there is an unexplained rise in temperature or abnormal pain.

Let us here, again, call attention to the word "débridement" which has been defined as the "excision of a wound." The term has degenerated in its application. Almost any form of wound cleansing has been called débridement—and wrongly so. Most doctors know what it means, and start such operations with every intention of being thorough. The skin and fat receive fair treatment. Then, many of us will begin washing the wounds to take away every bit of the evidence of deep-seated dirt. The rest of the procedure will be devoted to aimless picking and clipping of tags of muscle and fascia over its surface. To be sure, the wound will look clean. One can wash the hematoma and extravasated blood from the muscles of a dressed rabbit which has been shot, but it will still be riddled with bird shot, hair and material from the intestinal tract. The operation does not terminate because the work has been systematically completed, but because patience has been exhausted and one does not see anything more that can be done.

The importance of this method of dealing with compound fractures prompts us to cite the following case as an example:

Case Report.—T. S., age 24, was admitted to the hospital, February 5, 1937, with a compound fracture of the left leg at its middle third. It had resulted from a pile of bricks falling on the extremity.

General examination was not remarkable. The leg presented a laceration, four

inches long, at the site of the fracture. There was gross soiling of the wound. No history or evidence of bone protrusion could be obtained although the fractured ends were visible in the wound. Four hours after the accident, the patient was operated upon under general anesthesia. Débridement was carried out as outlined above. Upon inspecting the bone, gross dirt was found embedded in the periosteum at the point of fracture. It was removed according to the method described. Silk was used throughout. The closure was facilitated by accessory incisions which were later dressed with vaselined gauze. The leg was placed in a padded spica encasement and supported on a knee flexion-splint. Gas and tetanus bacilli antisera were administered and the patient returned to the ward in good condition.

The temperature curve showed spiking to 101° F. during the first three postoperative days. It then dropped to normal for one day, and spiked again on the fifth, sixth, and seventh days. At this time there was evidence of a moderately severe serum rash. The elevated temperature and increased pulse were not accompanied by an increase in respirations. The temperature promptly subsided with the rash. All sutures were removed at the end of two weeks, when the first dressing was made. The relaxing incisions were redressed and found to be nearly closed. The patient was discharged to the Fracture Clinic, February 23, 1937, to be treated as if he had a simple fracture.

It appears also worth while for us to cite a case illustrative of the value of immediate skin grafting in the primary closure of traumatic wounds. As was done in this case, many of these patients can be handled without admission as bed patients in the hospital.

Case Report.—R. M., age 47, entered the hospital, February 12, 1938, following an injury of the right hand, sustained while cranking an automobile. The engine had "kicked," causing the end of the crank to tear through the dorsal surface of the web between the thumb and index finger. The skin and subcutaneous fat were missing. The extensor pollicis longus tendon was exposed, the adductor pollicis muscle was almost completely mangled, and there was a compound fracture of the first metacarpal bone at its middle third.

Three hours after the accident, débridement was begun, under local anesthesia, with the realization that skin grafting would have to be done in order to close the defect. However, a bridge of extensor pollicis longus tendon across the wound had not been anticipated. It would have been better to have covered the wound with a flap of skin and subcutaneous fat from the abdominal wall. However, the patient could not stay in



FIG. 5.—Primary skin graft to cover a tendon exposed through loss of overlying tissues by the injury. See report of case. (Stevenson and Reid: *Am. Jour. Surg.*, 46, 442-449, December, 1939, Fig. 3.)

the hospital and, to simplify his care, a split-graft was removed from the thigh to cover the defect. Six weeks later he returned to his job as pressman in a print shop.

The photograph (Fig. 5) shows a very superficial position of the tendon. Although the graft is adherent to it, there is enough freedom in movement in other tissues beneath the graft to give the thumb a full range of function. It is doubtful whether this tendon would have survived any delayed form of grafting. The patient still refuses further correction.

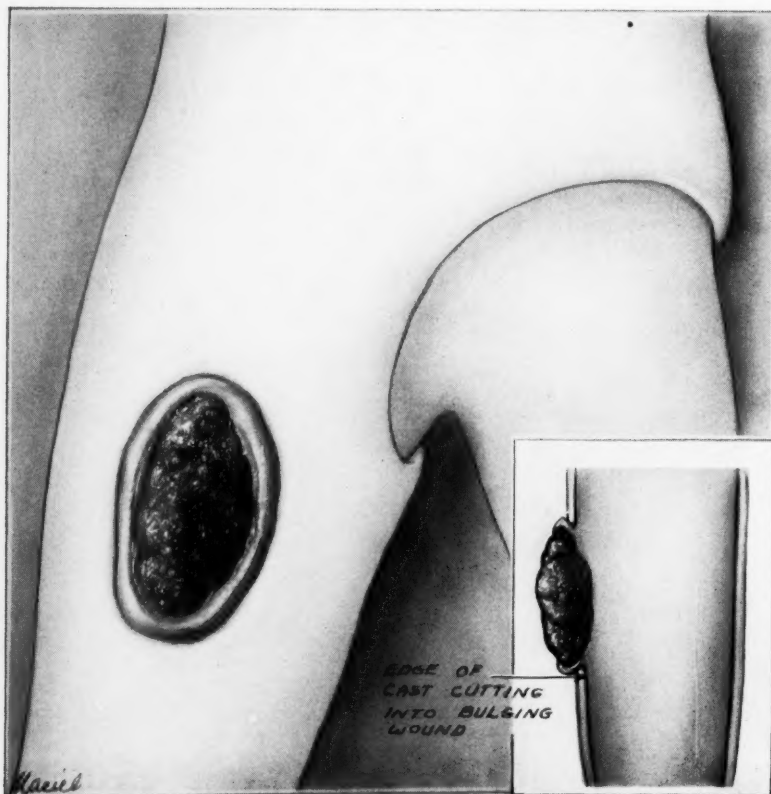


FIG. 6.—The effect on the underlying wound produced by cutting a window in the encasement over it. The circulation in the wound is interfered with, and its immobilization is destroyed.

It should be stated, however, that serious cases such as we have been describing may, if the patient's condition demands it, be postponed for a day or possibly two, after the débridement and cleansing, for delayed primary suture.

(5) *The treatment of traumatic infected wounds or contaminated wounds which, because of the exigencies of the situation such as often arise in war time, should have no attempt made at primary closure.* In war, the facilities at one's command, the conditions under which one has to work, and the lack of trained personnel often make it very unwise to attempt any primary closure of traumatic wounds. This was invariably the case in the Chinese war to which we have referred.

While most surgeons adopt an arbitrary time limit of six to eight hours in deciding whether a wound is contaminated or infected, we are influenced by the nature of the soiling, the location, and extent of the injury. For instance, we all know that we can take more chances that wounds about the head and face are only contaminated, even though they have exceeded our adopted time limits. On the other hand, we know that it was very unwise to gamble with contamination versus infection when the soiling was from Flanders fields or the trenches. When in doubt, smears from the tissue pieces might show large numbers of bacteria and thus throw the decision in favor of "infection." However, this section of our paper deals only with the preparation of fresh wounds, usually not over three days old, for healing by secondary intention, secondary closure, or skin grafting. Tetanus and gas bacillus antitoxin are always administered to such patients.

The field of operation is prepared as already described. A general anesthetic is much preferred. A tourniquet is used if possible. The wound is laid extraordinarily wide-open, so that no packs, drains, or tubes will be regarded as necessary. Foreign bodies and completely detached pieces of bone are removed and all recognizable dead or devitalized tissue cut away. It cannot be overemphasized that the success of this method is directly dependent upon the thoroughness of the débridement. Grease- and dirt-stained living tissues, particularly bone, tendons, and nerves, are completely cleansed with soap and water, using a scrub brush if necessary. This is followed by a most thorough washing with normal salt solution, using the gloved finger to massage the tissues gently. Following this, gowns, gloves, and instruments are changed; the skin is dried and recoated with merthiolate; new drapings are applied. The tourniquet is removed and bleeding vessels are ligated with very fine chromic catgut ligatures. Tendons and nerves are not sutured; there is no internal fixation of fractured bones. The wound is not even partially closed. It is filled with vaseline or with well-saturated vaselined gauze, or with both, and then so dressed as to be as absolutely immobile as it is possible to make it. The pressure of the dressing over the wound is made quite firm in order to combat the tendency toward edema in it. If possible, such a dressing is left undisturbed until the protection of a healthy granulation tissue is formed, or until the dangers of manipulation from removing the dressings are negligible. This usually means two weeks and may mean more than four weeks. Above all, we try to avoid dressing such a wound through a hole in an encasement which, because of the lessened pressure, will often allow the wound to become edematous and actually herniate through the encasement. This has always appeared to us to be a serious handicap to the healing of such a wound. We prefer, when the dressing has to be made, to remove the entire dressing and replace it with a new one.

Healthy and unharmed granulation tissue is such a good protection that we can see no reason for disturbing it until the time arrives when we wish to prepare it for secondary closure or skin grafting. This may be early or late, depending upon many circumstances, such as the complications of frac-

tures or osteomyelitis in the wound, or such as the equipment and personnel at the disposal of the surgeon. For such preparation of granulating wounds we prefer to use Dakin's solution, but that is another story which is beyond the scope of this paper.

Those of you who heard Doctor Matas at our meeting last year, or have read Winnett Orr's paper or J. Trueta's book, will recognize a familiar tone throughout this paper. Doctor Matas' description of the management of the war wounds in the Spanish Civil War was truly delightful. We want to close this paper with two quotations from the remarks he made at that time. The first is: "There, at the war front, rude experience imposed by necessity seemed to discount the importance of germs, provided the living tissues were allowed to fight their own battle unencumbered by the bodies of dead or dying tissues, and kept undisturbed and protected in the process of repair and reproduction from tempestuous manipulations and destructive germicidal irrigations by absolute fixation in plaster." The second is: "Suffice it to say, that when fresh wounds are relieved of all dead or devitalized tissues, they are, when put to complete rest, quite able to take care of themselves without the aid of antiseptics, which (when truly bactericidal) hinder the normal reproduction of the tissue cells and weaken their defenses."

This paper was read before the Fifty-third Annual Session of the Southern Surgical Association, Hot Springs, Va., December 10, 11, 12, 1940.

THE USE OF SULFANILYLGUANIDINE IN SURGICAL PATIENTS

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IN SEPTEMBER, 1940, Marshall and his coworkers published the results of their studies with sulfanilylguanidine.¹ Their paper described the method of preparation and the properties of this compound. They reported careful experiments on mice, rabbits and dogs, which were designed to compare the relative toxicity of sulfanilylguanidine with sulfapyridine and sulfathiazole. From these experiments it appears that this new sulfonamide compound, when given orally, is probably less toxic than sulfapyridine or sulfathiazole. The investigations of Marshall and his group brought out clearly two facts of possible significance for surgeons. They showed that, although sulfanilylguanidine is fairly soluble in water, it is poorly absorbed from the intestinal tract, and secondly, that the concentration of coliform bacteria in the feces of mice is greatly reduced after the oral administration of the drug. Furthermore, they found that the new compound is as active as sulfapyridine is against pneumococcus infections in mice, and from studies *in vitro* they showed that it is as effective as sulfanilamide is against several other pathogenic bacteria.

It was these observations that led us to consider using sulfanilylguanidine in the preparation of patients who needed operations upon the colon. The present paper is an account of our experience with this drug in 12 such cases.*

CASE REPORTS

Case 1.—H. G.: The first surgical patient upon whom sulfanilylguanidine was used had had a long and tedious experience with previous operations. She was age 39 when admitted to the Johns Hopkins Hospital. Eighteen years before a cyst had been removed from the left ovary. Seven years later an exploratory celiotomy was performed for partial intestinal obstruction. Three years thereafter a second cyst was removed from the left ovary. For the following seven years the patient had been comfortable but, then, periods of cramplike pain in the lower abdomen recurred. The persistence and severity of these attacks increased and became associated with distention, nausea and vomiting. Such was the account given by the patient of her illness, and efforts to obtain actual data bearing on the previous operations were of no avail.

The patient was admitted to the Gynecologic Service. The physical examination failed to reveal any deviation from the normal, except in the pelvic organs which were embedded in moderately firm adhesions. Several loops of intestine were thought to be attached to the left adnexae. With the patient under anesthesia, a mass was felt which was adherent to the left uterine cornu, and fixed to the left lateral wall of the pelvis.

Operative Note.—The abdomen was opened through a low midline incision. Part of the omentum formed a mass which was attached to the left side of the uterus and to a large ovarian cyst that was adherent to the left pelvic wall. After some dissection, it was found that the right tube and ovary were missing. A supravaginal hysterectomy was then completed, and it became evident that the left tube and a loop of intestine were

* The sulfanilylguanidine used in these studies was supplied by the Calco Chemical Company.

firmly attached to the ovarian cyst. Considerable bleeding was occasioned by the removal of these structures, upon completion of which the operator found a peculiarly narrow strip of intestine, which was devoid of mesentery, extending from the descending colon to the rectum. This loop of bowel was approximately eight inches long and, unfortunately, was open in two places. After considerable dissection, it became clear that the sigmoid had been removed previously, and that a segment of ileum had been interpolated to connect the descending colon and the rectum (Fig. 1). This nonviable,

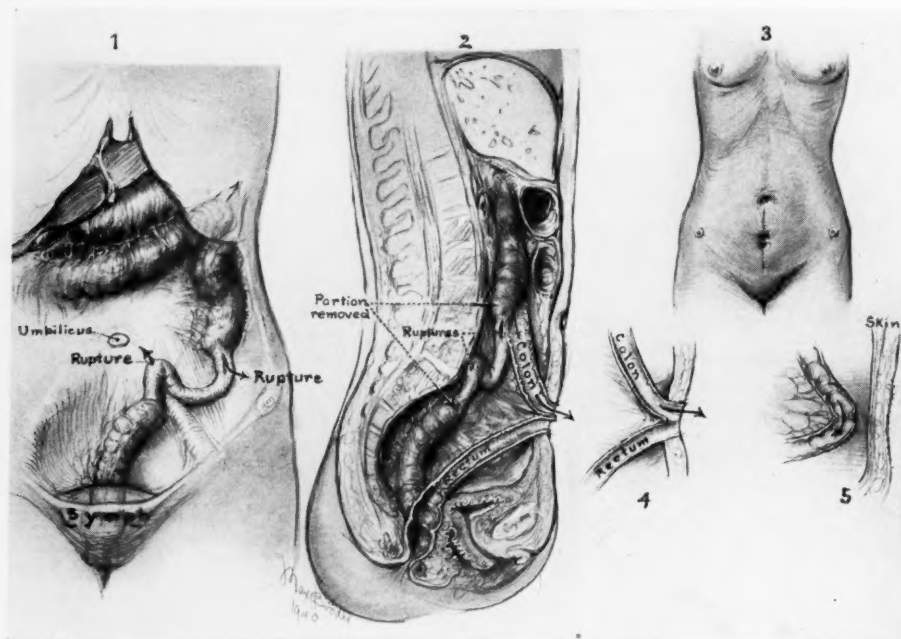


FIG. 1.—Case 1: Drawings illustrating the conditions present in this patient.

perforated loop of bowel was then resected, the end of the descending colon freed from adhesions and opened, and the upper end of the rectum mobilized and opened. The patient was showing the effects of the long operative procedure, and, as there had been considerable fecal contamination, the operator felt that an end-to-end anastomosis was out of the question. The open ends of the colon and rectum were then brought through the midline incision, and the wound closed above and below the openings. There was so little tissue available that a very short spur resulted from the approximation of the descending colon with the rectum.

The spur was subsequently removed and an effort made to close the colostomy with sutures. The tension between the loops was too great, and the wound broke open. At this point in the patient's convalescence she was given 7.5 Gm. of sulfanilylguanidine by mouth every day for one week. The concentration of coliform bacteria in the colonic discharge fell rapidly, and a second operative closure was attempted. At this operation the open ends of the colon and rectum were dissected from the abdominal wall, freed from adhesions and lengthened. The proximal and distal ends were joined by two layers of sutures. In carrying out this anastomosis there was gross soiling. The sutured bowel was replaced in the peritoneal cavity, and the abdominal wound closed with silk without drainage.

Only twice after the operation did the patient's temperature go as high as 100° F. On the fifth postoperative day she began to have normal stools and, except for cramp-like pain, her convalescence was uneventful. There was one very small stitch abscess which

cleared up in 24 hours after it was opened. The patient continued to receive sulfanilylguanidine every day for a week following the operation.

SUMMARY.—A patient, who after several previous operations, required a colostomy of the Mikulicz type, in which the afferent and the efferent loops were under tension. The colostomy was successfully closed and the bowel placed intraperitoneally despite gross fecal contamination.

Case 2.—C. M.: This vigorous, middle-aged white male, came to Johns Hopkins to have a colostomy closed. He gave the following account of his illness: On March 12, 1940, he was awakened by pain in the lower part of the abdomen. The intensity of the pain rapidly increased and was followed by nausea, vomiting, and fever. He was unable to work, which was most unusual for him. His family physician felt that an operation was imperative, and 18 hours after the onset of his symptoms a celiotomy was performed through a midline incision. The peritoneal cavity was found to be full of "milky fluid." There was a mass arising in the sigmoid. The segment of diseased bowel was removed. The patient was told that the lower end of the sigmoid adjoining the rectum had been closed and placed in the pelvis, and that the proximal end of the divided bowel had been brought through the abdominal wall in a separate incision (left pararectus). Subsequently the terminal end of the descending colon either retracted to form an abscess or became gangrenous. The patient only knows that the wound was badly infected, and that a second operation was required in order to have the colostomy function.

On admission he was seen to be an obese man in no apparent ill health. On examination the rectum was found to extend five inches above the internal sphincter. The colostomy opening was small and was surrounded by a broad area of dense scar tissue. The patient was given 4 Gm. of sulfanilylguanidine orally every eight hours for six days. A solution of the drug was used on three occasions as a retention enema to reduce the bacterial count in the rectum. At operation innumerable adhesions were encountered beneath both incisions (Fig. 2). The ends of the divided bowel were mobilized and the terminal portions excised to facilitate anastomosis. It was found that a sizable portion of the descending colon and most of the sigmoid were missing. The operator was forced to mobilize the hepatic flexure in order to obtain approximation of the colon to the rectum. In doing this the tension was so great that the colon was stretched and flattened; consequently a six-inch rubber tube one inch in diameter was placed in the lumen of the bowel and an anastomosis made around this tube. Interrupted sutures of catgut were used and wherever possible these were reinforced with Lembert sutures of silk. One could not be certain that the anastomosis was secure at any point. A Penrose wick was placed in the midline wound, and both incisions were closed with silk throughout. The cecum was then brought through a right McBurney incision with the expectation that it would be subsequently opened.

For nine days after this operation the patient received 4 Gm. of sulfanilylguanidine orally every eight hours. There was never any distention, there was no leakage from the anastomosis, and there was prompt and frequent passage of flatus and feces per rectum. On the ninth day after operation the patient strained and passed per rectum the large rubber tube that had been supporting the line of anastomosis. Previously the lower end of this tube had been barely palpable by digital examination. The complete absence of distention made the opening of the cecostomy quite unnecessary. Both abdominal wounds healed promptly without infection. Following the operation the patient's temperature only once was above 100° F., and was entirely normal after the fourth postoperative day. His pulse rate ranged between 90 and 100 for three days and thereafter was in the 80's. He left the hospital three weeks after the operation.

SUMMARY.—Previously a resection of part of the descending colon and most of the sigmoid had been performed. The distal end of the sigmoid had

been replaced in the pelvis. An open tube anastomosis was carried out, restoring the continuity of the large bowel. The anastomosis healed *per primam*.

Case 3.—W. B.: A white male, age 73, who had been treated previously in the Johns Hopkins Hospital for generalized arteriosclerosis, arteriosclerotic heart disease and hypertension, was readmitted, complaining of a gastro-intestinal upset. Upon questioning it was found that three months before he began to experience gastric pain an hour and one-half after meals. The pain persisted until the following meal. In addition he had had cramps in the lower bowel which sometimes awakened him. The bowel move-

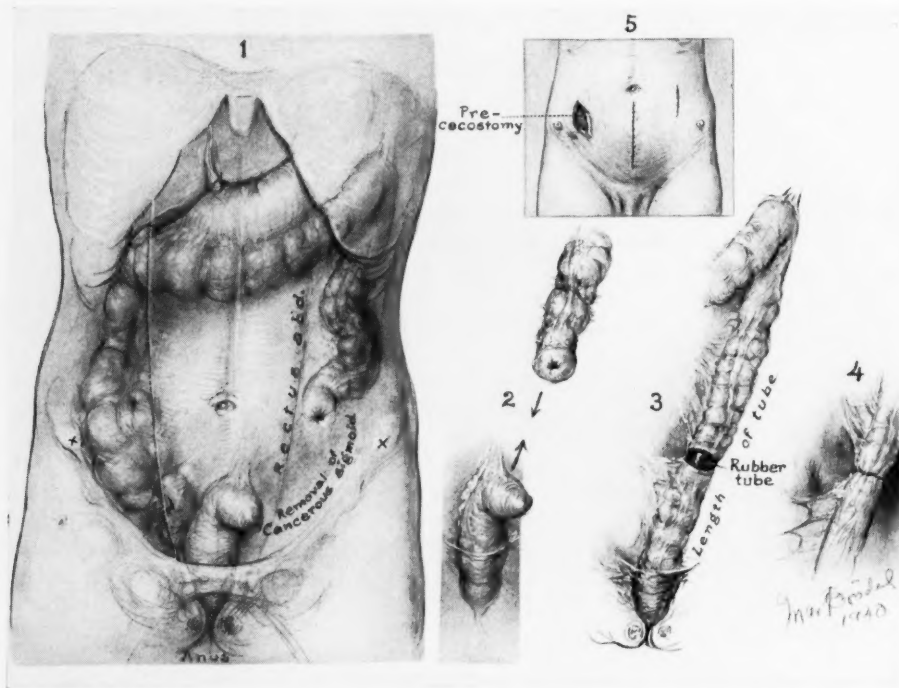


FIG. 2.—Case 2: Drawings illustrating the conditions present in this patient.

ments had become watery and loose, and at times his stools had been dark. The patient had tried various diets without any success. One week before coming into the hospital he had two short attacks of pain radiating along the course of the right ureter. He described the pain as intense, otherwise his history was unessential. On physical examination, there were obvious evidences of arteriosclerosis, the heart was enlarged to the left, there was a precordial systolic murmur, and tenderness on palpation in the lower part of the right side of the abdomen. His blood pressure was 210/110. He was thoroughly studied on the Medical Service. A barium enema showed a persistent filling defect in the ascending colon below the hepatic flexure. The characteristics of the defect strongly suggested the diagnosis of malignancy. There was also evidence of adhesions around the cecum.

Upon questioning, the patient gave the additional information which proved to be of the utmost importance. Forty-three years before, while on a bicycle trip through France, he had an attack of acute appendicitis. An appendiceal abscess formed and ruptured into the cecum. No operation was performed. The patient had had no subsequent indication of infection in this region.

He was given 4 Gm. of sulfanilylguanidine by mouth every eight hours. On the fourth day the patient became drowsy and cyanotic. He was thought to be showing signs

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of toxicity, like those seen in sulfanilamide poisoning. The daily blood levels of combined sulfanilylguanidine had been running between 4 and 4.5 mg. per cent. At the time of his drowsiness, the blood level was found to be 23.6 mg. per cent. Investigation showed that the patient had been given 24 Gm. of sulfanilamide by mistake. This drug was obtained from his urine, and analyzed by E. K. Marshall, Jr. The patient continued to receive sulfanilylguanidine following the error, and daily blood level determinations showed after 48 hours that the concentration of sulfanilylguanidine had returned to 4.5 mg. per cent.

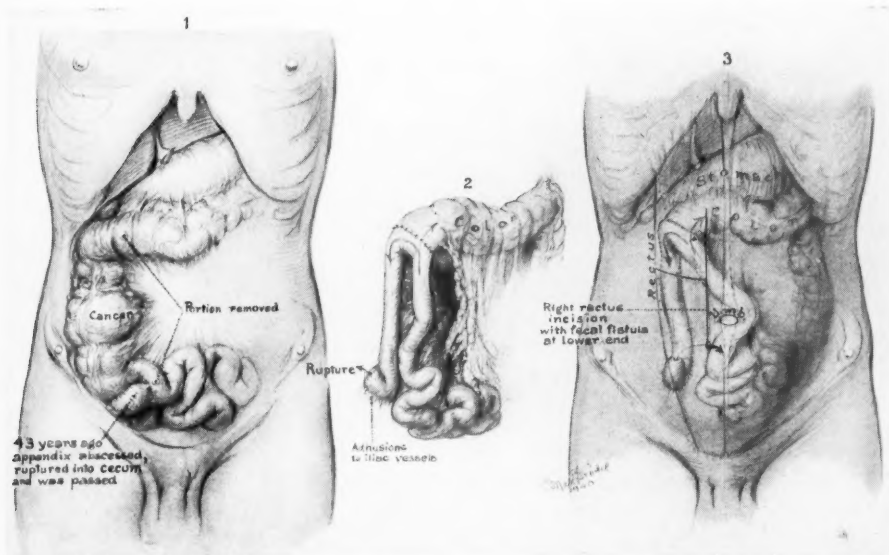


FIG. 3.—Case 3: Drawings illustrating conditions present in this patient.

After seven days of preparation by chemotherapeutic agents he was operated upon. There was a large carcinoma just below the hepatic flexure which was fixed to the parietal peritoneum. The nodes in the mesentery were enlarged and firm. There were many short, tough adhesions at the site of the appendiceal abscess. The terminal ileum and its mesentery were closely attached to the common iliac vessels (Fig. 3). The operator divided the terminal ileum about 2 cm. from the ileocecal valve, and resected the right side of the colon, removing the tumor and the mesentery. The patient's cardiovascular condition was not particularly good at any time, and it was a question whether to attempt to dissect the terminal ileum from its attachment to the common iliac vessels, or to invert the stump and establish a lateral anastomosis between the ileum and the transverse colon. The removal of the tumor had been tedious and the dissection had been difficult. It seemed wise, therefore, to shorten the time of operation as much as possible; consequently, the end of the transverse colon was sutured to the ileum about 18 cm. above the inverted end of the terminal ileum. The wound was closed with silk throughout. No drains were used.

For five days after the operation the patient did surprisingly well. Only once did his temperature go above 100° F., and within 48 hours after the operation his temperature was normal and remained so. His pulse rate varied between 88 and 104. There was some distention, but he had bowel movements. On the sixth day the lower angle of the incision opened, discharging both gas and fecal matter. It seemed clear that the sutured end of the terminal ileum had opened and that a fecal fistula had developed. A very surprising feature in this case is that the patient had given no signs of peritonitis. He had no abdominal pain or tenderness. There was no fever or tachycardia and, although the

wound had been closed tightly, the lower angle opened spontaneously to accommodate the discharge from the terminal ileum.

During the five days after the operation he had continued to receive 12 Gm. of sulfanilylguanidine by mouth each day. When the fecal fistula developed, he was given sulfathiazole intravenously and later by mouth. His subsequent course is uneventful except for the development of an abscess which opened through the upper angle of the wound. The fistula is closing slowly at the present time.*

SUMMARY.—Carcinoma of the ascending colon in an elderly patient suffering from arteriosclerotic heart disease and hypertension. Forty-three years before, an appendiceal abscess had spontaneously ruptured into the cecum. A right-sided resection was carried out, with an ileotransverse colostomy. A fecal fistula developed from the terminal ileum.

Case 4.—L. D.: An obese white female, age 57, came reluctantly to the Johns Hopkins Hospital. Her previous experience with surgery elsewhere had been most discouraging. In July, 1936, after months of discomfort, she was operated upon for hemorrhoids and "inflammation" of the cervix. Following this she complained of indigestion, eructation and weakness. In October of the same year, a second operation was carried out. The patient was told that the appendix was diseased and had had to be removed. Furthermore, adhesions around the gallbladder had been freed and a dermoid cyst involving the left ovary and colon necessitated an oophorectomy and a partial colectomy. After the operation the patient found herself with two incisions—a low midline one and a high left rectus one, through each of which the divided end of a loop of colon protruded. Her convalescence was uncomfortable; a purulent discharge from the rectum was present which required irrigations through the lower colostomy. Fever and attacks of pain continued for five months, terminating promptly when a gauze sponge was extruded from the left rectus incision. This necessitated a plastic operation to insure proper function of the colostomy. For 18 months the patient was free from symptoms, and then she had the first of seven attacks of acute intestinal obstruction. Each attack was relieved by good nursing care. The last obstruction was so obstinate, however, that she was forced to seek surgical aid.

On examination, one found that the patient had two abdominal scars (Fig. 4) each of which marked the site of a large ventral hernia containing many loops of small intestine. The distal end of the severed colon had retracted beneath the low midline scar and was completely closed; the proximal end of the colostomy was functioning.

The patient was given sulfanilylguanidine orally 4 Gm. every eight hours for eight days, together with a low residue diet and daily enemata through the colostomy.

At operation, there were, of course, extensive adhesions between the loops of intestine, both in the hernial sacs and in the abdominal cavity. The disparity in the caliber of the proximal and distal ends of the colon was so great that an end-to-end anastomosis seemed inadvisable. The continuity of the colon was reestablished, therefore, by a lateral anastomosis. This was carried out by the open technic and, despite the preoperative enemata, fecal matter was extruded during the operation. When the anastomosis was complete, the colon was placed within the peritoneal cavity, a Penrose drain was put in the lower angle of the midline incision, and both wounds were closed with silk throughout. The operation took over three hours, but a transfusion and the administration of fluids intravenously prevented any detectable evidence of shock.

On the day of operation, the patient was given 4 Gm. of sodium sulfathiazole intravenously and 4 Gm. of the same drug by mouth. The following day she was given 12 Gm. of sulfanilylguanidine, but an extensive macular rash developed over the entire body. It was thought that this was the result of sulfathiazole, and for 24 hours the

*Two weeks after the meeting of the Southern Surgical Association this patient contracted bronchopneumonia and passed away.

drug therapy was suspended. The rash persisted and in order to eliminate sulfanilylguanidine as a causative agent, this drug was resumed in the same dosage as before, and continued for eight days, during which time the rash completely disappeared. The patient's convalescence was noteworthy for the absence of distention and for the prompt and perfect healing of both wounds. She was discharged 15 days after the operation.

SUMMARY.—Previous resection of part of the descending colon with double colostomy. Two ventral herniae were repaired with silk and the continuity of the colon restored by an open anastomosis. Healing *per primam*.

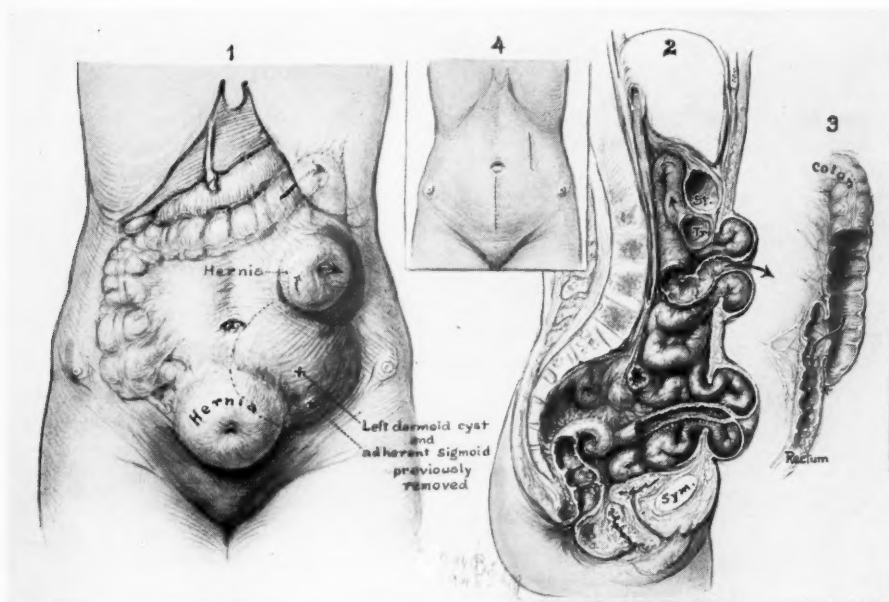


FIG. 4.—Case 4: Drawings illustrating conditions present in this patient.

Case 5.—D. T.: This emaciated white female, age 66, was a patient of Dr. Harvey Stone. She had had a long-standing illness of ulcerative colitis, for which an ileosigmoidostomy had been performed three years before the present admission. This operation was followed by a period of relative well-being, but for the last six months she had complained of diarrhea, chills, fever, malaise, and had lost 20 pounds in weight. When admitted to the hospital she was obviously acutely ill. During the first week of residence there her temperature varied from 98° to 102° F., her pulse rate from 100 to 130, and her blood pressure was 100/40. There was a large tender mass in the lower part of the left side of the abdomen. Sulfanilylguanidine was given in doses of 3.3 Gm. every eight hours for ten days before operation.

A left rectus incision was made, and in an effort to mobilize the mass that had been palpated the operator broke into several abscess cavities. The transverse and part of the descending colon had become gangrenous and had perforated in at least three places. There was a gastrocolic fistula. The walls of the stomach were so edematous that the closure of this fistula was unsatisfactory. The operator was finally able to deliver the gangrenous portion of the colon and to establish a Mikulicz colostomy. A drain was placed through a stab wound in the lower part of the abdomen. Throughout the operation the patient's condition was precarious, and two transfusions and intravenous fluids had to be given; the following day a third transfusion was needed. At this time it was noted that the urinary output was greatly diminished. There were casts which had not been present before. Three days after the operation the patient became

jaundiced and continued to have a meager urinary output. The progress notes recorded each day the absence of distention. There were no signs of generalized peritonitis, and by the third day after operation the pulse rate had fallen to 100 and the temperature to 99.8° F. Only once during the week after operation did the patient's temperature rise above 101° F. During the second week of convalescence she had a chill and fever after the intravenous administration of glucose solution. The renal function gradually returned to normal and her convalescence continued satisfactorily.

SUMMARY.—Resection of gangrenous colon. Closure of a gastrocolic fistula in the presence of abscesses without developing a generalized peritonitis.

The preceding cases were complicated ones that required detailed description. We have used sulfanilylguanidine in seven additional patients whose histories are briefly abstracted in the following paragraphs.

Case 6.—L. C.: An obese colored female, age 58, came to the hospital complaining of constipation and blood in the stool. The past history was noncontributory. The illness that brought her to the hospital began two months before admission, at which time she passed a large amount of bright red blood per rectum. For the following week she had diarrhea, each stool containing blood and mucus. Thereafter she had alternately diarrhea or constipation, marked tenesmus, and discomfort in the lower abdomen. There had been no loss of weight. The physical examination was negative. There were no evidences of intestinal obstruction. A barium enema, however, showed a large filling defect in the lower portion of the descending colon. The patient was given 7.5 Gm. of sulfanilylguanidine a day for nine days before the operation was performed. An annular carcinoma of the sigmoid with metastasis to the regional nodes was found. This was removed, and an end-to-end anastomosis, with an aseptic technic, was carried out. At the same time a cecostomy was established. Following the operation she was given sulfanilylguanidine for a week. Her convalescence was uneventful, except for a moderate degree of fever which persisted for six days. At no time, however, did her temperature go over 101.6° F. The cecostomy closed spontaneously. She had effectual enemata from the third postoperative day and normal spontaneous bowel movements after the seventh day.

SUMMARY.—Annular carcinoma of the descending colon in an obese, colored female. An aseptic end-to-end anastomosis was performed. Healing *per primam*.

Case 7.—E. D.: A white male, age 19, had survived a severe automobile injury 18 months before admission to the hospital. At the time of the accident he suffered a fracture of several ribs and a left hemothorax. The patient gradually recovered, but six months later developed increasingly severe signs of partial intestinal obstruction. At the time of admission he was greatly distended. He had lost 60 pounds in weight, and was having constant cramplike pain and vomiting. A barium enema showed a definite obstruction at the splenic flexure of the colon. The abdominal cavity was opened and an enormous dilatation of the transverse colon, terminating in a benign stricture at the splenic flexure, was found; accordingly, a cecostomy for decompression was made. Two weeks later he was again operated upon, and the left half of the transverse colon, the stricture, and a portion of the descending colon were resected. The walls of the transverse colon were so edematous and friable that it appeared unlikely they could hold sutures; consequently, the proximal and distal segments were brought out on the abdominal wall side-by-side, in the manner of a Mikulicz resection. The disparity in the caliber of these two ends was striking, the proximal loop being three times as large as the distal one. After the clamps had come off, the larger segment gradually shrank in size; but even after the spur had been crushed the colostomy did not close. It became evident that operative measures would be necessary in order to close the colostomy. In preparation for the operation the patient was given sul-

fanilylguanidine. He received seven doses of 4.5 Gm. at 12-hour intervals. At operation it was necessary to open the peritoneal cavity in order to mobilize the proximal and distal ends of the colon. The anastomosis was carried out in the presence of gross fecal contamination; nevertheless, no evidence of peritonitis appeared. The wound healed promptly and completely, except for a very tiny fistula that subsequently closed. Beginning 24 hours after the operation, the patient was given 4.5 Gm. of sulfanilylguanidine by mouth every 12 hours for four days.

SUMMARY.—A posttraumatic stricture of the splenic flexure, requiring resection and secondary colostomy; closure necessitating intraperitoneal suturing in the presence of feces.

Case 8.—I. S.: This patient was a colored female, age 49, who was admitted to the hospital with a story that suggested the presence of a carcinoma of the sigmoid. The physical examination and barium studies confirmed this impression. She was prepared by the usual colonic regimen and by the administration of sulfanilylguanidine. She received 12 Gm. by mouth daily for five days. At operation a large carcinoma of the sigmoid involving also an adjacent loop of ileum, was found. The entire tumor and adjacent sigmoid, together with the segment of ileum, were removed in one piece. An end-to-end aseptic anastomosis of the sigmoid and a lateral open anastomosis of the ileum were then performed. The abdominal wound was closed without drainage. A prececostomy was provided, but was never opened. The patient had a smooth convalescence, her temperature reaching 100.4° F. on only one occasion. The drug was continued for nine days after the operation, during which time the patient was entirely free from distention. Her wound healed *per primam*, and she left the hospital on the fifteenth postoperative day.

SUMMARY.—Carcinoma of the sigmoid involving the ileum. Block resection of sigmoid and ileum with aseptic anastomoses.

Case 9.—V. S.: A colored male, age 25, came into the hospital with symptoms and signs of acute appendicitis. At operation, the appendix was thought to be inflamed and was removed. Further exploration showed that the sigmoid and two separate areas in the ileum were involved by acute regional enteritis. Preparation had not been made for resection, and the patient's condition became so precarious that the abdomen was closed without further intervention. He ran a febrile course for two weeks following the operation. He complained of abdominal tenderness and cramplike pains. The wound drained small amounts of seropurulent fluid but never any fecal material. He was then prepared by the use of sulfanilylguanidine (9 Gm. daily for four days), and a resection of the terminal three feet of ileum and the right side of the colon was carried out. During this operation a small abscess beneath the cecum was opened. An end-to-side ileotransverse colostomy was performed, by an aseptic technic, and the wound closed tightly with silk. The patient made a smooth recovery, his temperature never rising over 100° F. The drug was continued for a week after the operation. The abdominal wound healed quickly without the slightest evidence of infection.

SUMMARY.—Regional enteritis involving three segments of the intestinal tract. Resection and anastomosis in the presence of a small abscess.

Case 10.—V. T.: A colored male, age 32, complained of frequency and dysuria. He had lost 25 pounds in six months. The physical examination showed a large, poorly defined mass in the right iliac fossa. A barium enema brought out displacement of the rectum toward the left. While on the ward the patient developed progressive distention and intermittent abdominal pain. He was given sulfanilylguanidine (12 Gm. daily for five days). At operation, he was found to have a large extraperitoneal tumor in the right side of the pelvis. Numerous loops of ileum were densely adherent to the tumor, and there was marked dilatation of the intestine above the adhesions. Attempts to free

the intestine were unsuccessful. The distention was relieved by performing an ileosigmoidostomy, with the open technic. The wound was closed with silk, without drainage. The postoperative course was remarkably smooth. The patient was discharged on the fifteenth day, his wound entirely healed, and his obstruction relieved.

SUMMARY.—Intestinal obstruction caused by a large retroperitoneal tumor, probably sarcoma. Open anastomosis between the ileum and the sigmoid.

Case 11.—I. D.: A white female, age 59, came into the hospital with symptoms that indicated she was suffering from a carcinoma of the transverse colon. The physical examination was consistent with this diagnosis. She was prepared for operation by the usual colonic regimen, and was given sulfanilylguanidine (7.5 Gm. daily for six days). At operation, a large carcinoma of the transverse colon was found. This was densely adherent to the cecum. Resection from the terminal ileum to the left side of the transverse colon was performed, and an end-to-side ileotransverse colostomy carried out by an aseptic technic. Her course was smooth for eight days. She then developed fever (103° F), without corresponding elevation of the pulse rate. There was localized tenderness in the left lower quadrant, but no evidence of peritoneal irritation. Her temperature gradually returned to normal, the abdominal tenderness disappeared, the wound healed *per primam*, and she had daily numerous bowel movements; the same trend of events repeated itself on the thirteenth and twenty-fourth postoperative days. No mass ever developed, and the highly localized character of the tenderness suggested an inflamed diverticulum of the sigmoid. There was never any tenderness in the upper abdomen at the site of the ileocolostomy, and never any evidence of generalized peritonitis.

SUMMARY.—Carcinoma of the transverse colon necessitating extensive resection and end-to-side anastomosis. *Per primam* wound healing and satisfactory bowel function. Three spells of fever and abdominal tenderness, probably due to diverticulitis.*

Case 12.—S. M.: A white male, age 26, complained of abdominal pain, diarrhea, and blood in the stools. Barium studies showed an irregular filling defect in the cecum. The patient was prepared in the usual manner for a colonic resection, and was given sulfanilylguanidine for three days preoperatively. At operation, a number of polypi were found in the cecum. The right side of the colon was resected, and a lateral ileotransverse colostomy performed, by the open technic. The drug was continued for six days after the operation. The patient's convalescence was smooth. His temperature did not rise above 100° F. at any time. The wound healed *per primam*. He was transferred on the fifteenth day to the Medical Service for the study of a microcytic anemia.

SUMMARY.—Polyposis of the cecum. Resection of the right side of the colon, with open lateral anastomosis.

In each of the foregoing patients, determinations were made in Marshall's laboratory to ascertain the concentration of sulfanilylguanidine in the blood. More than 90 determinations were made with average total values of from 2 to 4 mg. per cent. In only two instances was the total blood level as high as 5.0 mg. per cent.

Similarly, in all the patients the concentration of coliform bacteria in the stool was studied before and after the administration of sulfanilylguanidine. This was done by making an emulsion of 1 cc. of stool with 9 cc. of P.D. broth. Serial dilutions in the ratio of 1:9 were made from this emulsion. One-tenth of a cubic centimeter of each mixture was added to a tube of desoxycholate agar and poured into sterile Petri dishes. After 48 hours' incubation at 37° C., the

* Subsequently, this was confirmed at operation.

SULFANILYLGUANIDINE

number of colonies in each plate was counted. In every patient the concentration of coliform organisms was reduced after the administration of sulfanilylguanidine, but this reduction was not consistent, and much additional study is necessary to determine accurately the effect of this drug on the intestinal flora of human beings. In Case 4 the estimated number of coliform organisms per cubic centimeter of stool fell from 16,720,000 to 10,000 after the drug had been given for 14 days. It is to be borne in mind, however, that this is the most extreme change that we have observed, and, furthermore, this patient received sulfathiazole intravenously and by mouth in addition to the sulfanilylguanidine.

A conscientious effort was made to detect any evidences of toxicity in the patients who received sulfanilylguanidine. Although the drug was given by mouth, none of the patients complained of nausea or vomiting. Case 3, who received 24 Gm. of sulfanilamide by mistake, continued to take sulfanilylguanidine without any ill effect. It is also noteworthy that in Case 4 a most extensive rash developed from the use of sulfathiazole. This rash faded promptly after the withdrawal of the compound, despite the fact that sulfanilylguanidine was continued over eight hours. This series of 12 patients is too small to permit one to make any statements about the toxic manifestations that may result from the use of sulfanilylguanidine.

The dosage of sulfanilylguanidine has varied in the patients reported in this paper. We have come, however, to give an oral administration of 50 mg. per kilo of body weight every eight hours as the standard dose. We believe that it is necessary to continue this amount of the drug for at least a week before any operative procedure is attempted, and in every case it is necessary to correlate the administration of the drug with the bacterial count before planning a resection of the large bowel.

SUMMARY

This presentation of the records of 12 surgical patients, who received sulfanilylguanidine before operations upon the colon, is to be looked upon merely as the initial step in a far-reaching clinical study. It is not justifiable to formulate any conclusions from such a meager number of observations. One can, however, in all fairness, contrast the postoperative progress of each patient receiving sulfanilylguanidine with the progress that might have been expected had the drug not been given. From this point of view, it seems highly probable that Cases 3 and 5 would have died if the concentration of coliform bacteria had not been reduced before operation. Furthermore, it is almost certain that without the use of sulfanilylguanidine the intestinal wounds in Cases 1, 2 and 4 would have failed to heal *per primam*. Of the remaining seven patients, only two can be regarded as significant in estimating the value of sulfanilylguanidine for large bowel surgery. These are Cases 10 and 12, upon whom open anastomoses were successfully performed without the slightest evidence of subsequent infection.

The convalescence of the patients described in this report justifies the impression that sulfanilylguanidine is a real adjuvant in colonic surgery.

The chief value of this study is the fact that it points to a new field of usefulness for chemotherapeutic agents that possess the properties of sulfanilylguanidine.

The author wishes to thank Mr. Max Broedel for the illustrations which were made from the written records of the operations.

REFERENCE

- ¹ Marshall, E. K., Jr., Bratton, A. C., White, H. J., and Litchfield, J. T., Jr.: Sulfanilylguanidine: A Chemotherapeutic Agent in Intestinal Infections. *Bull. Johns Hopkins Hosp.*, 67, 163, 1940.

DISCUSSION.—DR. LEO BRADY (Baltimore, Md.): Through the courtesy of Doctor Firor, and his associates, I have had the opportunity of using this drug in two patients. The first was a female, age 25, in whom an endometriosis had been mistaken for carcinoma of the sigmoid, with involvement of the uterus. When I saw her, the uterus and ovaries and six or eight inches of intestine had been removed and a colostomy performed. She was only 25 years old, and was not content to continue with the colostomy; she was willing to have anything done to overcome that. She was given this drug for eight days. At operation, I was unable to effect any type of regular anastomosis, so I employed the technic advocated by Balfour 25 years ago, of uniting the ends over a rubber tube and bringing the tube out through the anus. I intended to establish an artificial intussusception, as Balfour recommended, but was unable to do more than bring the two open ends into apposition. The patient had no vomiting, no nausea and a perfectly uneventful recovery.

The second patient had recurring Hunner's ulcers, bilateral hydronephrosis and a contracted bladder. I treated her by fulgurating the ulcer, but the bladder was so contracted that each time this was done it was necessary to anesthetize her. Finally, she developed stones in the left ureter. She was given sulfanilylguanidine; the stones were removed and the left ureter implanted into the sigmoid. She had a slight elevation of temperature for a few days, but no signs of peritonitis. I operated upon her two weeks ago. She still has bladder incontinence but can control the urine that she passes through the rectum. In a few weeks I intend to implant the right ureter into the rectum.

Neither of these women had any nausea nor vomiting, and were able to resume taking the drug almost as soon as they came out of the anesthetic.

DR. HARVEY B. STONE (Baltimore, Md.): Through the kindness of Doctors Firor and Marshall I have employed this drug in six cases. I shall not go into details, but there was involvement of the colon of one kind or another in each case. They have all survived operation. I think one at least belongs in the category of the "circus case" you saw in Doctor Firor's picture. There was a perforation between the colon and the stomach as a result of long-standing colitis, and, in addition to that, a perforating abscess at the splenic flexure. She survived the operation, which seemed an impossibility at the start, and she has gone home well. How much value to attribute to the drug it is hard to say. Several of the cases were the routine cases you expect to get well anyhow. They all did well with the drug. It will require a lot of additional experimental work to really evaluate it.

I want to emphasize a few points to which Doctor Firor called attention. The drug possesses the two remarkable and more or less contradictory properties of being more readily soluble in water than any other sulfonamide

compound, and, on the other hand, is less absorbable from the alimentary tract. Ordinarily, one thinks the property of absorbability as being in proportion to the property of solubility. In this case it is not. In addition to these physical properties, it apparently has a more specific attack on the colon group of organisms than any other drug. The combination of these three qualities—the solubility in water, the lessened absorbability from the alimentary tract, and the specificity for the colon group—obviously, make it an agent almost ideally designed for attack upon the bacterial flora of the large bowel. There is one other point in its practical administration I should like to point out. You apparently get the highest degree of effectiveness at the end of six or seven days of administration. It takes about that time of preliminary administration of this drug to insure the fullest bacteriostatic effect in the colon group of organisms, and this effect rapidly disappears when the drug is withdrawn; and after several days of cessation of giving the drug, the bacteria reappear rapidly. Therefore, it seems wise to give it for six or seven days prior to the planned operation and to continue the administration of the drug six or seven days after operation, until wound healing in the suture line has progressed to the stage where the alteration in the bacterial count is no longer of significance.

I would like to ask Doctor Firor to say more about the dosage. I think we have been giving 4 Gm. of the drug twice a day.

DR. ARTHUR M. SHIPLEY (Baltimore, Md.): Several weeks ago, Doctor Firor was good enough to put this drug at our disposal at the University Hospital. Dr. Monte Edwards is especially interested in surgery of the rectum and colon, and he reported to me, a few days ago, that he had recently resected the sigmoid for carcinoma and had performed an open end-to-end anastomosis without any subsequent evidence of infection in the wound. He reported also that there had been the same amazing drop in the bacterial count during preparation prior to operation.

DR. FRANK H. LAHEY (Boston, Mass.): Have there been noted any contraindications or any evidences of toxicity in the use of this drug?

DR. WARFIELD M. FIROR (Baltimore, Md., closing): With reference to the degree of absorption, we have found that the blood level concentration ordinarily runs between 2 and 4 mg. per cent, and in only two instances did it go over 5 mg. per cent. The dosage was experimented with in this group of patients, and at present we feel that 50 mg. per kilo of body weight every eight hours for a week before operation and a week after operation is a perfectly safe amount to give. In some experimental work, it has been found that far better results are obtained by giving the drug at eight-hour intervals than more frequently or in a single large dose.

In answer to Doctor Lahey: I can only say that we have been on the lookout for evidences of toxicity or contraindications to the use of this drug, and have not found any. I talked to Doctor Marshall just the day before yesterday. He has been using sulfanilylguanidine in a series of patients with bacillary dysentery with splendid results, when it is given in the first three days of illness. This report will appear in the January issue of the Bulletin of the Johns Hopkins Hospital.

In summary, we feel that we are just at the beginning of our experimental studies on the use of chemotherapeutic agents in the large bowel.

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PNEUMONECTOMY*

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THE PRESENT STATUS of pneumonectomy is somewhat analogous to that of partial gastrectomy during the years immediately following the first gastric resection by Billroth. In the minds of many of the medical profession—physicians and surgeons alike—the operation pneumonectomy connotes a dramatic and ill-advised undertaking accompanied by a terrific surgical attack and fraught with unwarranted hazards. It is the purpose of this communication to refute such ideas and to relate a personal experience with 18 cases of complete pneumonectomy and subtotal resection of the lung. This work has been undertaken chiefly at Bellevue Hospital, and it is here, also, that Cournand^{4, 5} and Maier⁹ have been carrying out their physiologic, and Miscal¹⁰ his anatomic, studies. According to autopsy statistics carcinoma of the stomach and intestine are the most frequent forms of cancer, and these are followed by carcinoma of the lung, which has an incidence of about 10 per cent of all malignancies found at necropsy. Like cancer elsewhere, carcinoma of the lung invades, metastasizes, and is fatal unless removed early. Unfortunately, irradiation therapy, whether by radium or roentgen ray, is of little or no avail. Gastric resection for cancer of the stomach is not only accepted but uniformly recommended as the procedure of choice by the medical profession. In St. John's, Whipple's and Raiford's¹⁶ series of 18 cases, 430 (59.8 per cent) were explored, with a 32.1 per cent mortality; and only 9, 1.3 per cent of the total, or 23 per cent of the resections, were alive at the end of five years. In Abrahamson's and Hinton's¹ series of 444 cases, 148 (33.3 per cent) were operable, and in only 16.2 per cent of these, or 5.4 per cent of the total, was gastric resection possible. Of the operated cases 77 (50 per cent) were operative mortalities. Although the various reported series of pneumonectomies for cancer of the lung are, of course, much smaller than the above and cover much shorter periods, still the results compare most favorably.

In 1939, Overholt¹² published a list, collected from the literature, of 58 pneumonectomies for malignant tumors; there were 38 deaths, or a mortality of 65.5 per cent. At the same time he reported his own series of 15 cases with five deaths, a 33.3 per cent mortality. In 1940, he¹¹ published his personal series of 75 cases of carcinoma of the lung, in which the diagnosis had been proved histologically. In 38 (50.6 per cent) of these, exploratory thoracotomy was performed; the mortality is not stated. In this group, 17

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pneumonectomies were performed with six deaths (35 per cent). Of these pneumonectomies, ten were complete, with individual ligation of the hilar structures, in four, mass ligation of the hilum was performed, and in three, the technic was not stated.

In a series of 86 pneumonectomies for cancer reported by Ochsner and DeBakey,¹¹ including seven of their own, there was an operative mortality of 64 per cent, and a recovery of 36 per cent. In 31 of these cases, there was individual ligation of the hilar structures, in 17, there was mass ligation at the hilum, and in the others, the technic is not clearly stated. Reinhoff¹⁵ gives a mortality of 10 per cent in 20 cases.

Historical.—Pneumonectomy was first suggested by Truc, in 1881, although he never attempted it himself. His suggestion, however, may have been based upon the experimental work of Gluck, in 1881, who showed that animals survived the operation. Quoting Carter, *et al.*³: "In 1892, Hassler, after the removal of one lung in a dog ten weeks old, found that the remaining lung, after six months, completely filled the thorax, and showed histologically normal structure with alveoli of normal size."

Mohlgaard and Roosing (1910) recognized that true hyperplasia of the remaining lung following pneumonectomy occurred only in young animals as against a compensatory dilatation in the adult animals.

In 1910, Kummel performed the first human pneumonectomy. This was for carcinoma, and the patient died on the sixth day. Following this, occasional pneumonectomies were performed unsuccessfully for bronchiectasis and suppuration, two of which were reported by Lilienthal, until 1931, when Nissen reported a successful pneumonectomy, by mass ligation, for bronchiectasis. Graham and Singer reported the first successful operation for bronchogenic carcinoma in 1933, and were promptly followed, in the same year, by Rienhoff and then by Overholt, with similar successful results. Since then the list has grown steadily. In April, 1935, Lyle⁸ presented a patient before the New York Surgical Society upon whom he had performed a pneumonectomy for carcinoma. Now pneumonectomy is performed without undue risk and with increasing success for pulmonary cancer, suppuration and bronchiectasis, and, occasionally, for tuberculosis.

Terminology.—Even to-day, the term *pneumonectomy* is so loosely used that it may signify either of two quite distinct operative procedures: first, it may mean the removal of the lung by the technic of mass ligation of the hilum of the lung *within the pleura*. This may result in amputation of the lung across the hilum just within the pleura, or, as is much more frequent, a tourniquet is placed about the hilum and a varying fringe of lung tissue remains after the pneumonectomy—partial or subtotal. There is still another type of procedure whereby, for example, the right middle and lower lobes are first removed and then, at a later date, a lobectomy of the right upper lobe is also performed. True, all of these methods describe some form of pneumonectomy, but I believe the proper terminology for any such procedure should be *pneumonectomy intrapleural* or *pneumonectomy sub-*

total. These are absolutely different procedures from a complete pneumonectomy performed *within the mediastinum* by opening the mediastinal pleura, with individual ligation of the hilar structures, and with removal of such lymph nodes as may be possible. In my opinion, the terms *pneumonectomy* or *complete pneumonectomy* should be reserved for this type of operation. This is important because in going over the reports of pneumonectomies one encounters a confusion of technics and terms. Pneumonectomy for cancer should always be complete, with individual ligation of the artery and veins, bronchial closure, and removal of as many of the bronchial nodes as possible. If the hilum of the lung is not sufficiently free to permit this, the case is inoperable, as the growth has already extended beyond the reach of surgery. In tuberculosis also, when pneumonectomy is contemplated, it should be complete. With bronchiectasis and pulmonary suppuration, however, intrapleural subtotal pneumonectomy may be, and in fact usually is, the procedure of choice and may be accomplished in one or several stages.

Anatomy.—Comparatively little attention has been given to variations and anomalies of the vessels at the hila of the lungs. It is stated in the ordinary anatomic descriptions that the pulmonary artery may sometimes divide within the pericardium, that occasionally there may be three pulmonary veins on the right or a single one on the left, and the bronchial arteries vary from one to three on each side. In one instance, we have encountered three veins on the right. Recently, Harris and Lewis⁶ cited the case of a patient in whom an anomalous branch from the aorta, about the size of the celiac axis, entered the left lower lobe through the broad ligament. Some years ago, we encountered an identical anomaly during the performance of a right lower lobe lobectomy. We have been interested in the variation in size and length of the pulmonary artery and veins, and in the shape of the latter. Occasionally a vein appears as a conical prolongation of the auricle and, furthermore, the pericardium may be extremely thin about the veins. Miscall has made a number of dissections in the fresh cadaver with this in mind, and has demonstrated to us considerable differences in the lengths and arrangements of the vessels and their first branches and the prolongation of the pericardium on the veins. In all surgery about the hilum of the lung such variations should be kept in mind and anomalous vessels sought for.

Physiology and Mechanics.—There are two interlocking questions, the answers to which are of vital concern to these postpneumonectomized patients: (1) What happens to the pleural cavity after removal of the lung?; and (2) what happens to the remaining lung? If there is no infection the pleural cavity is normally obliterated, as Rienhoff¹⁵ says, by a prompt rise of the diaphragm; slight curvature of the spine, with a falling downward and inward of the ribs; some shift of the mediastinum to that side, with compensatory emphysema of the opposite lung; marked thickening of the parietal pleura; and the gradual organization of the plasma, which fills the space after operation so that a loose mesh of organized fibrin and fibrous tissue results. In this meshwork small collections of fluid may persist. It has

been our practice to aspirate the pleural cavity postoperatively, as often as necessary to relieve symptoms and to keep the intrapleural pressure within or near normal limits. Rienhoff also thinks that the compensatory emphysema of the opposite lung is partly hypertrophy and partly simple dilatation of the air sacs without rupture or destruction of the elastic tissue as occurs in true emphysema.

Studies in embryology and comparative anatomy show that actual growth of the lung continues after birth, probably until about the seventeenth year. Carter and Longacre,³ and later Longacre,⁷ have been working on this problem from the physiologic aspect with pneumonectomized puppies and adult dogs for seven years. At the end of three years, their results seemed to show that following pneumonectomy the adult dogs developed emphysema sufficient to impair their activities, whereas after nine months the puppies compensated as well as their controls when subjected to similar stress. At the end of seven years, however, Longacre feels that eventually the puppies developed evidence of emphysema in comparison with their controls. On the clinical side, Graham and Overholt both have patients carrying on their usual occupations over five years after pneumonectomy; one had a thoracoplasty and the other did not. It will only be by a careful follow-up of such patients that we shall learn whether or not to advise a thoracoplasty to prevent overdilatation of the opposite lung and symptoms of emphysema or fibrothorax.

For several years, under the direction of Richards, Cournand,^{4,5} and Maier, we have been carrying on studies along similar lines with tuberculous patients both before and after surgery. Recently, we have included also our pneumonectomy group. These procedures include:

(1) *Lung Volume Measurements*: These are divided into vital capacity and residual air, the sum of which form the total capacity. Normally, the vital capacity forms about 75 per cent of the total capacity, and the residual air 25 per cent, varying somewhat with sex and age. "Increase in the proportion of residual air and decrease in the proportion of vital capacity may indicate pulmonary fibrosis, congestion of the lung, emphysema (compensatory or pathologic) or presence of a poorly ventilated air pocket in the lung."

(2) *Breathing Capacity*: This is less well-understood, and "is the measure of maximum ventilation per minute or maximum breathing capacity. In other words, it tests the efficiency of the chest bellows for air displacement."

(3) *Ventilation under Varying Physical Activity*: This is estimated "(a) under basal conditions; (b) during a one-minute period of exercise; and (c) during the period of recovery following it."

(4) *Breathing Reserve*: "The breathing reserve is the excess breathing capacity, beyond the actual ventilation used."

(5) *Efficiency of Ventilation*: "From each liter of air circulating in the lung a variable amount of oxygen is removed by circulating pulmonary blood, during rest, exercise and recovery. In pathologic states, poor coordination between aeration and blood perfusion of the lungs, or parts of the lungs, may result in inefficient ventilation."

(6) *Study of Respiratory Gases in Arterial Blood*: "In normal subjects at rest and during early recovery of the standard exercise, the arterial blood leaving the lung is between 94 and 98 per cent of the maximum oxygen saturation. Values below this range usually mean that a certain proportion of the blood has circulated through the improperly ventilated alveoli." These estimations, also made in the immediate postoperative period, are of considerable prognostic aid and are of great help in the application of oxygen therapy.

(7) *Study of the Circulation*: "To test the capacity of the heart and pulmonary vascular bed to accommodate an increased blood flow, to test, that is, for any latent pulmonary congestion we have used the venous pressure-infusion test. In this, the level of venous pressure and the vital capacity are followed during the course of a rapid intravenous infusion. If the vital capacity decreases significantly during this infusion it is evidence of congestion in the pulmonary vascular bed, due either to a local state of the capillaries or to an obstacle to the flow of blood in the pulmonary veins, or to latent left heart failure. If the venous pressure shows an abnormal increase there is suggestive evidence of embarrassment of the right side of the heart under the conditions of the test."

Preoperatively, we think that, together with the other clinical and usual laboratory observations, such studies help us estimate the risk of surgery to the patient and, at six-month intervals postoperatively, we feel that we are enabled to gain a better insight into the respiratory and cardiorespiratory status of these pneumonectomized patients. Our work has hardly begun, and we realize that it will take several years to evaluate our results.

A brief résumé of and comments upon the 18 cases may be of interest:

ABBREVIATED CASE REPORTS

(A) PNEUMONECTOMY FOR CANCER

Ten Cases

Case 1.—J. M., male, age 52, had noticed a cough, with yellowish sputum for a year. Seven and five months previously he had had severe hemoptyses. During the three months prior to admission he had lost 25 pounds in weight, and had become weak. Roentgenograms showed a large, solid mass in the right lower chest. Bronchoscopy was not undertaken. Operation revealed a large tumor occupying most of the right lower lobe. The lung was free and the hilum normal. A complete pneumonectomy was performed. As the bronchus was ligated the patient suddenly died. *Histologic Diagnosis*: Bronchogenic carcinoma. *Comment*: Peribronchial novocain injection might have prevented this fatality.

Case 2.—T. M., male, age 45, had noticed sharp pain under his right scapula and in right upper arm for about three months, and there had been a loss of 25 pounds in weight. Roentgenograms showed a solid, spherical mass in the left midchest, well away from the hilum. Bronchoscopy was not undertaken. Operation disclosed a completely free and normal hilum. This was dissected, the vessels and bronchi ligated, and the bronchial stump sutured. In the lower lobe there was a firm mass adherent to the posterior chest wall. The remainder of the lung was not adherent. On removing the lung, it was found that the mass in the lower lobe was invading the pleura and ribs. *Histologic Diagnosis*: Bronchogenic carcinoma.

The patient made a smooth postoperative recovery, and was completely relieved of his pain. The wound healed cleanly. He did not gain weight, and six weeks after

operation developed a transverse myelitis. He died on the forty-seventh day from spread of his tumor.

Case 3.—T. G., male, age 43, had complained of blood-streaked sputum for two months before admission. Bronchoscopy with biopsy revealed a bronchogenic carcinoma in the right middle lobe bronchus. Roentgenograms of the bones were negative. Operation revealed a small tumor at the mouth of the middle lobe bronchus. The mediastinal nodes were enlarged and firm. Complete pneumonectomy was performed, together with a dissection of the mediastinal nodes. The patient made an uneventful convalescence, and the wound healed cleanly. One month later a metastasis was noted in the second right rib. This was removed, and radon seeds implanted. The patient went home but returned to the hospital very shortly, and pursued a downhill course, with intense pain in his right shoulder. A cordotomy was performed which gave relief during the remainder of the patient's life, which was only three weeks. The patient died seven months after his pneumonectomy.

Autopsy showed recurrence of the tumor in the right pleural cavity and ribs on the right side, with involvement of the sympathetic chain on the right and several thoracic vertebrae.

Case 4.—R. B., male, age 60, had noted a "wheeze" in his left chest for three years, and a slight cough, with mucopurulent sputum, occasionally blood-streaked, for one year. Nine months before admission he developed pleurisy in the left chest from which 200 cc. of straw-colored fluid was removed. Two months before admission he was bronchoscoped and a tumor noted in the left main bronchus. On admission to the hospital, he was rebronchoscoped, with similar findings. The biopsy was reported as a bronchogenic carcinoma, transitional cell. Complete pneumonectomy was performed. The lower lobe showed extensive suppuration and bronchiectasis beyond the tumor. The patient had a very stormy convalescence, due to auricular fibrillation and the development of pneumonia in his right lung, from which he finally recovered only to develop an empyema in his left pleural cavity. This was drained, with a rib resection. At one time there was a small bronchial leak which persisted only a few days. At the time of operation a group of large aortic nodes were removed. No evidence of tumor was found in any of the nodes but on removing them the recurrent laryngeal was injured. He was finally discharged from the hospital, eight months postoperative, without any sign of recurrence. The reason for his prolonged hospital stay was that he had no place to go. After seven months' drainage the empyema sinus closed.

Case 5.—W. R., male, age 55, had a history of symptoms for ten months, starting with gripe and a persistent cough, with about 90 cc. sputum a day. There had been a loss of 30 pounds in weight. He had been attending the Bellevue Hospital Medical Clinic for four months. He was then admitted to the hospital and observed for 17 days before bronchoscopy was undertaken, which revealed a tumor in the right main bronchus just below the middle lobe opening. Biopsy showed carcinoma, transitional cell. Operation was delayed because of an upper respiratory infection. Sputum cultures showed *Streptococcus haemolyticus* and *Streptococcus viridans*. A complete pneumonectomy was performed five weeks after admission. There were enlarged mediastinal lymph nodes. The patient developed an extensive pneumonia, and died 48 hours postoperative. In the operative specimen, the bronchial nodes on section showed extensive tumor infiltration but there was none found in the deeper nodes. *Comment:* Operation should have been delayed and the patient should have received sulfapyridine immediately before and after operation.

Case 6.—E. B., male, age 31, developed a cough one year before admission and, during the interval, there had been several episodes of hemoptysis. Roentgenograms, seven months before admission, were reported negative. Others, taken one month before admission, showed a density throughout the left lung, with retraction of the mediastinum to the left. He had coughed about 90 cc. of sputum a day throughout his illness, and there had been some dyspnea on exertion throughout the year. There was no weight

loss. After admission, bronchoscopy showed a mass in the left main bronchus. Biopsy report was bronchogenic carcinoma, transitional type. A complete pneumonectomy was performed three weeks after admission. No enlarged mediastinal nodes were noted, but as the hilum was dissected it was found that a tongue of tumor extended up along the posterior wall of the trachea beyond the carina. Inasmuch as this had not been noted on preliminary palpation and the vessels had all been ligated, pneumonectomy was completed. The bronchus was ligated and sutured at the level of the trachea, but a small piece of tumor on the posterior wall of the trachea was left *in situ*. The patient made an uneventful convalescence, and the wound healed cleanly. He was discharged one month postoperative. He has gained weight since, and when last seen, four months postoperative, was still well. He was complaining of a dry cough at that time, and bronchoscopy showed the end of the bronchial ligature protruding into the bronchus. Inasmuch as this was well embedded in the tissue it could not be pulled out. No mediastinal enlargement was seen roentgenologically at that time. The patient had resumed work.

Case 7.—W. J., male, age 54, gave a six months' story of loss of weight, vague substernal pain, and recent hoarseness and sore throat. Roentgenograms showed a shadow in the right middle lobe. He was bronchoscoped twice. The first was reported as negative, and the second showed the presence of a tumor in the right middle lobe bronchus; biopsy from which was reported as bronchogenic carcinoma, squamous cell. A complete pneumonectomy was performed. The lung was entirely free; there was no involvement of the mediastinal nodes; and the tumor was found, as described, in the right middle lobe bronchus. The patient made an uneventful convalescence, and the wound healed cleanly. Convalescence was complicated by an infection in one eye and also by a cystitis, both of which cleared up. He was discharged to the convalescent wards on the fifty-second day, and has since shown no sign of recurrence.

Case 8.—M. A., male, age 37, had noticed pain in his right shoulder and upper arm for six months. There had been a dry cough for two months. No loss of weight. Roentgenograms revealed a large, homogenous and well-circumscribed shadow in the upper part of the right upper lobe. Bronchoscopy was not undertaken. Operation revealed a large, solitary yellowish tumor in the right upper lobe, adherent on the mediastinal side and at the apex. A complete pneumonectomy was performed. As the lung was removed, it was evident that particles of tumor were left along the innominate vein and subclavian vessels on the right. The patient did very well for 12 days when his bronchial stump broke open, following which he developed an empyema. He went rapidly downhill, and suffered intense pain in the right shoulder and arm which could not be relieved. Cobra venom, alcohol injections and morphine were all ineffective. He died on the forty-second postoperative day.

Autopsy showed an extensive recurrence of the tumor in the right pleural cavity, involving the vertebrae, mediastinum, parietal pleura, and bronchial stump. No tumor elsewhere in the body. The tumor was reported in the operative specimen as a hypernephroma. Kidneys and adrenals, however, were normal at autopsy. It is possible, therefore, that this may have been an anaplastic type of bronchogenic carcinoma.

Case 9.—I. S., female, age 33, had no relevant previous history. A dense shadow in the left upper lobe was discovered in taking routine roentgenograms while searching for a focus of infection to account for a choroiditis. Bronchoscopy was not undertaken. Physical examination was negative for nodes, but showed marked dullness over the left apex. Aspiration biopsy was reported as showing a chronic inflammatory process. A complete pneumonectomy was performed. There were extensive adhesions to the anterior chest wall and along the mediastinum. It was at first thought that these were not due to invasion of the tumor; therefore, the operation was completed, inasmuch as the hilum was entirely free. In removing the lung, however, it was found that the tumor had invaded the anterior chest wall and that there was a group of enlarged subcoracoid nodes.

Therefore, along with the lung, the intercostal bundles and muscles of the first, second, and third spaces, together with the second and third ribs, were removed from the sternum to the midaxillary line, together with the group of nodes beneath the coracoid. The patient made a rather slow convalescence, and her wound healed cleanly. Before discharge she was given 2,300 r units of roentgenotherapy. The tumor was reported histologically, as a reticulum cell sarcoma. The patient left the hospital on the forty-second day.

On July 1, 1940, about two months postoperative, there was no evidence of recurrence either by palpation or roentgenologically, but the patient still had pain in the back of her chest, probably due to retraction and high negative pressure. This was in part relieved by injection of alcohol into the fourth, fifth, sixth, and seventh intercostal nerves. Five months postoperative, the mediastinum appeared normal, and she had gained weight, but a small, firm node had appeared above the left clavicle.

Case 10.—V. W., male, age 63, had an hemoptysis ten months before admission, followed by a month of daily cough with blood-streaked sputum, during which time he lost between five and ten pounds of weight. Three months prior to admission, he began to have inconstant blood-streaked sputum, since which time he had lost between ten and 15 pounds. On admission to the hospital, he was found to have a lesion involving the upper part of the left upper lobe. This could not be seen by the bronchoscope. At operation, a tumor was found which was operable. A complete pneumonectomy was performed. Convalescence was uneventful except for undue pain and a rather bizarre white count running between 4,000 and 16,000, with 10 to 25 per cent polynuclears.

In reviewing these ten cases, first, the anterior approach was employed in all; and, second, there were two operative deaths—one during operation and one two days later of pneumonia. The first mortality might have been prevented by injecting novocain about the main bronchus, which we have done since. The second, in view of his recent respiratory infection and sputum cultures, should have had his operation postponed, and have had sulfapyridine administered just prior to and following surgery. Three died of their tumors in from 42 to 210 days after operation. The bronchial stump leaked temporarily in one instance, and broke open in a second, due to tumor invasion.

In one case, fluid had been present in the chest. This, however, was due to pneumonia and not to the tumor *per se*. I do not feel, therefore, that the presence of fluid necessarily precludes surgery, unless tumor cells can be demonstrated, the fluid is bloody, or there are other frank signs of pleural metastases.

Of these ten cases, only two patients (Cases 7 and 10) can be considered as ideal. Of the five who now survive, one had extensive suppuration and bronchiectasis at the time of pneumonectomy; one had an irremovable extension of cancer along the posterior wall of his trachea; and one had extensive invasion of her chest wall and lymph node metastases. Yet all of these patients were greatly benefited by operation—one was working four months later; another was living comfortably in a permanent home; and the third is with her family, leading a somewhat restricted life, and will undoubtedly require further radiation therapy. The two theoretically ideal cases were of men in their sixth and seventh decades, and appeared to be somewhat older than their stated ages. Neither has a home, and because of their general arterial status their future is problematic. One is in a convalescent home and the other about to go to one.

In passing, it might be of interest to mention the exploratory thoracotomies for cancer in which pneumonectomy was found to be impossible. During this same 17-months' period 14 such procedures were performed by the staff. There were two deaths from empyema; in both instances specimens for biopsies from the lung had been taken. All of the other patients made prompt recoveries with very little reaction from their operations. One patient even returned to his work as a carpenter, although his pleura was covered with metastatic nodules and the hilum "frozen." One additional patient, age 60, was explored because a bronchoscopic biopsy had been reported to be carcinoma. At operation, a large, firm mass involving the hilum was found. In attempting to free this the superior vena cava was torn, with fatal results. Autopsy disclosed the mass to be a tuberculoma. Needless to say, if the biopsy diagnosis had been correct, surgery would not have been attempted, and, furthermore, the case should have been recognized as inoperable. Finally, there were 18 patients with a proven diagnosis, by biopsy, of bronchogenic carcinoma, who were considered unfit even for exploration—all of these died while in the hospital.

Thus, of the total 42 patients with cancer of the lung, all except six from a municipal hospital, 66.6 per cent seemed to warrant exploration; and in ten instances, 33.3 per cent complete pneumonectomy was feasible. We should be able to look forward with considerable assurance to a definite betterment of these statistics.

(B) BRONCHIECTASIS AND SUPPURATION

Six Cases

Case 11.—G. W., male, age 23, with extensive bronchiectasis and suppuration throughout left upper and lower lobes, productive of 840 cc. of foul sputum a day, even after bronchoscopic treatment and pneumothorax. A complete pneumonectomy, with individual ligation and suture of hilar structures, was performed. *Result:* Death from pneumonia and empyema, 72 hours postoperative.

Case 12.—J. H., male, age 26, with extensive suppuration of his entire right lung. He had been under bronchoscopic treatment for three months. A complete pneumonectomy, with individual ligation of the hilar structures, was performed. *Result:* Death on the twelfth day of sepsis, empyema, and eventual leakage of the bronchial stump.

Case 13.—M. K., male, age 36, with extensive cystic bronchiectasis of entire right lung. A subtotal intrapleural pneumonectomy was performed. *Result:* The patient developed an empyema, the remaining stump of lung dilated, and the mediastinum shifted sufficiently to fill the chest, which had shrunk markedly in size. One year later, the patient has a small amount of morning sputum, but is otherwise well.

Case 14.—S. K., male, age 28, with chronic suppuration in left lower lobe following a lung abscess. A lobectomy was performed. Following this, his suppuration extended to the upper lobe, and, eventually, this lobe was removed. He is now awaiting thoracoplasty to close his empyema.

Case 15.—K. G., male, age 37, who had suffered from diffuse bronchiectasis in his right lung since a crushing injury of the chest five years previously. Bronchoscopy showed a stricture of the main bronchus. Operation revealed a healed fracture of the right main bronchus, with resulting stricture. A subtotal intrapleural pneumonectomy was performed. The patient made a smooth convalescence, without infection of any sort. He is awaiting further studies to determine the advisability of thoracoplasty.

PNEUMONECTOMY

Case 16.—S. G., female, age 27, had suffered from dry bronchiectasis of the left lower lobe for years with frequent attacks of pneumonia. Roentgenograms showed what was considered to be a large cyst of the left upper lobe. Operation revealed a large thin-walled cyst occupying the entire upper lobe. This communicated through a very minute opening with the lower lobe, which was completely fibrosed about a group of very large thick, dilated bronchi containing only a small amount of secretion. Except for the communication with the lower lobe there was no demonstrable bronchus to the upper lobe. Subtotal intrapleural pneumonectomy was performed. The patient recovered without infection. She is now awaiting a decision as to thoracoplasty, because of a small bronchial leak that developed two months after operation.

As it so happened, in this small group all the subtotal intrapleural pneumonectomy patients recovered and the two with complete pneumonectomy succumbed to the operation. It is fair to say, however, that these two had highly infected and grossly suppurating lungs at the time of operation and hence were most precarious operative risks.

(c) TUBERCULOSIS

Two Cases

Case 17.—N. N., male, age 34, had had an extensive two-stage extrapleural thoracoplasty of eight ribs, and an apicolysis, on the right. His apical cavity still remained open. After several months of sanatorium care, a complete pneumonectomy with individual ligation of the hilar structures was performed, after bronchoscopic examination showed the main bronchus to be normal. Following operation the patient exhibited extreme dyspnea, and died on the third day. During this period his arterial oxygen did not drop below 85 per cent but in spite of this and an oxygen atmosphere of 60-70 per cent his dyspnea persisted.

Autopsy failed to show a cause of death. The pleura was clean, the bronchial stump tight, and the other lung free of disease. This suggests true mediastinal flutter, which might have been controlled by tight packing, inasmuch as firm closure of the chest wall was impossible due to the former thoracoplasty.

Case 18.—M. S., female, age 32, who had been operated upon many times because of a mixed infection empyema and bronchial fistula. Inasmuch as her fistula and positive sputum persisted she requested pneumonectomy. The bronchus was the site of a healed tuberculous stricture, and there was moderate contralateral infiltration. Complete pneumonectomy with individual hilar ligation was performed, and the chest firmly packed. She did rather well at first but then developed increasing dyspnea and signs of bronchopneumonia in the opposite lung and died on the ninth postoperative day. Roentgenograms showed what we thought to be an exacerbation of her tuberculosis.

Notwithstanding these two fatalities I feel that pneumonectomy is indicated in certain selected cases of pulmonary tuberculosis, more especially those with a healed stenosed bronchus. This should always be complete with individual ligation of the hilar structures. Probably the mortality will always be higher in this group.

Summary.—A history of the development of the operation pneumonectomy has been given briefly and its application to certain types of disease described.

The anatomic, mechanical, and physiologic factors that should be considered have been discussed.

Eighteen clinical cases have been summarized, in which pneumonectomy has been performed during the period between May 1, 1939, and October 1,

1940. In ten of these, the operation was performed for cancer, with two operative deaths. Complete pneumonectomy was performed in each instance.

In six, the operation was performed for bronchiectasis, suppuration, or cystic disease. There were two operative deaths. In both of these a complete pneumonectomy was performed; in the other four, a subtotal intrapleural pneumonectomy was the procedure.

The third group comprises two cases of advanced chronic pulmonary tuberculosis. Both died.

A comparison is given of the results of surgery for cancer of the stomach and of the lungs. The operative mortality is less for exploratory thoracotomy and pneumonectomy than it is for exploratory celiotomy and gastric resection for cancer.

CONCLUSIONS

(1) The term "pneumonectomy" as used at present is inexact. There should be more specificity; hence "complete pneumonectomy" and "subtotal" or "incomplete intrapleural pneumonectomy" are suggested. As to complete pneumonectomy, I am in full accord with Rienhoff when he says: "No lung or peribronchial tissue or lymph nodes should be left behind. If such is the case a complete pneumonectomy has not been performed." This always means individual ligation of the vessels and closure of the bronchus within the mediastinum.

(2) In cancer, when a pneumonectomy is considered, it should always be *complete*. Intrapleural mass ligation of the hilum is to be condemned. Again to quote Rienhoff: "Only those patients in whom the lung is, in the main, free from the chest wall, and the hilus uninvolved, should be subjected to operation, otherwise a relatively safe surgical procedure will be brought into disrepute."

(3) Pneumonectomy is the procedure of choice in certain cases of bronchiectasis, cystic disease, or suppuration. It may be either complete or subtotal intrapleural. Probably the latter will be safer in the majority of instances because of the possibility of infection.

(4) When pneumonectomy is indicated for pulmonary tuberculosis, it should always be complete. This will lessen the danger of dissemination of the disease and persistent bronchial fistulae.

(5) Operative mortality statistics for pneumonectomy should be clearly differentiated: First, according to the disease—cancer, bronchiectasis and suppuration, or tuberculosis; and, second, as to whether or not the pneumonectomy was complete or a subtotal intrapleural procedure.

(6) There is but little in the literature about vascular anomalies of the hila of the lungs. These should be recorded when encountered.

(7) It is important to study the respiratory and cardiorespiratory physiology of patients after pneumonectomy, in order that we may advise, and treat more intelligently, this growing group of patients. These studies should be threefold: (1) as an aid to ascertain the operative risk of the patient; (2) to

study the patient subsequent to pneumonectomy; (3) to determine, eventually, whether or not a thoracoplasty should be recommended following pneumonectomy.

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DISCUSSION.—DR. HOWARD LILIENTHAL (New York): The paper by Doctor Berry is an important one from many points of view. The exact definition should be noted: The significance is total removal of the lung with its section within the mediastinum and with no pulmonary tissue remaining. But Doctor Berry admits that, in cases neither cancerous nor tuberculous, the operation may be performed intrapleurally. It should then be specifically designated.

Discussion of all the divisions of the paper would be impossible at this time. For example, the study of measurements of volume, respiratory capacity, ventilation, study of arterial blood and of the circulation in general, might well form the subject of an entire volume. Although I am incapable of doing more than to bring the subject to your attention, it is well that Doctor Berry has shown the importance of studying these branches of pathology and physiology in most of the cases which come to the attention of the surgeon, both before and after operation. And, naturally, one should be, so far as possible, acquainted with abnormal anatomic facts, particularly, the vascular—arterial and venous—irregularities.

In the technic of the operation itself—pneumonectomy—it is the surgeon's art which may well determine the result, as distinguished from his knowledge of the scientific aspect which he must learn from those who work with him.

Practically all of this has been discussed in the paper itself, and I mention it now so that the operation itself may not occupy the "center of the stage."

The sudden death of a patient during an intended pneumonectomy has been mentioned. I believe that this misfortune is more frequently observed during intrathoracic procedures than in other operations. I have had this accident happen in two of my cases—in both during ligation of a bronchus. In a third, not one of intended pneumonectomy, I had used an exploring needle to locate, if possible, a metallic foreign body. The "dead" patient came to life after long-continued artificial respiration. He still has the foreign body in or near the mediastinum and I have refused to make further efforts to relieve him surgically of the cough, which he thinks persists because of the presence of the offending little bit of metal.

Whether the employment of a local anesthetic would prevent this accident, it would be impossible to *prove*, even though there were a large number of cases. And, too, there is always the possibility of idiosyncrasy.

The patient in Doctor Berry's series, who coughs because of the presence of a rather long thread of silk within the bronchus, might, perhaps, be relieved by electrocautery through the bronchoscope.

As to intrapleural pneumonectomy in suppurative disease, it seems to me well worth contemplating, because, especially here, complete removal of the diseased parts is not so imperative as it is in cancer or tuberculosis.

DR. HERBERT C. MAIER (New York) said that he and Doctor Cournand had been investigating various physiologic disturbances and readjustments following pneumonectomy. The patients have been studied before operation and at varying intervals after pneumonectomy. In the immediate postoperative period, one of the problems has been the arterial oxygen saturation, which indicates whether the blood is well oxygenated during its passage through the pulmonary circuit. In those cases in which the patient had a very satisfactory clinical course, it was found that the oxygen content of the arterial blood returned to a normal level within a few days following pneumonectomy. In cases with emphysema or with some complication in the postoperative period, the readjustment is somewhat slower and may take several weeks. These studies of the determination of arterial oxygen have been used as a guide as to how long oxygen therapy should be continued. To rely upon clinical criteria, such as dyspnea and cyanosis, is not satisfactory; these signs are too inaccurate to be a reliable guide as to whether oxygen deficiency is present.

Obtaining blood for arterial oxygen saturation determination is a relatively simple procedure. Blood is usually obtained from the brachial artery and the procedure, once mastered, is no more difficult than the obtaining of blood from a vein.

As for changes in pulmonary function some months following pneumonectomy, final conclusions are not available at present. In those cases in which the tumor was located in a main bronchus, and the lung had undergone considerable atelectasis before operation, the respiratory function is changed very little by the pneumonectomy. An important factor is the relatively slight thoracic deformity which follows uncomplicated pneumonectomy.

A point of great interest, is whether there is actual destruction of the elastic tissue and the early development of emphysema in cases of pneumonectomy in which the organization of fluid results in a marked retraction of the mediastinum and an associated increased size of the remaining lung. We are studying these patients at intervals of several months after operation. The time interval is at present too short for us to draw any final conclusions, but it is Doctor Maier's hope that by continuing the observations it will be possible to arrive at a possible answer to the question whether, in some cases, thoracoplasty should follow the pneumonectomy, in order to diminish the extent of mediastinal deviation and to lessen the effect that the displacement may have on the contralateral lung.

DR. CARL EGGERS (New York) brought out the fact that several cases shown by Doctor Berry in his paper, indicated that decided progress had been made in thoracic surgery during the last few years. This presentation should be stimulating to all of us. The technical problems of the radical operation of pneumonectomy have been largely mastered. It is a very difficult operation, one should not lose sight of that. Doctor Neuhof touched upon the possibility of treating some patients by a procedure less exten-

sive than a total pneumonectomy. It is only a small group of cases in which that will be possible. Personally, I have had only one patient with an intralobar carcinoma in whom an upper lobectomy was sufficient. These cases are very apt to have a pleural invasion, and become inoperable from that standpoint.

The greatest technical advance in performing pneumonectomy has been made since Rienhoff stressed the importance of treating the structures of the hilum by individual ligation through an anterior incision. Aside from the importance of the proper technic, however, there are those physiologic problems to consider that Doctor Berry touched upon, and which his coworkers have emphasized. They are not clarified as yet, and progress is still, undoubtedly, going to be made. Then there is another phase which we must not lose sight of, *i.e.*, that in these carcinoma patients we are dealing with cancer which, in the lung, presents the same characteristics as in other organs. We must emphasize the importance of getting the patients early. Just as in carcinoma of the breast or stomach, if the patients are operated upon and the lung resected before the lymph nodes are involved, a fair percentage of recoveries may be looked for. It is surprising how long it takes before the diagnosis is made in most of these cases. Both clinicians and roentgenologists must learn to interpret symptoms and findings accurately and earlier, then we may hopefully look into the future for better results.

DR. CHARLES W. LESTER (New York) said that with regard to pneumonectomy in children, that some of the most brilliant results are going to be found in this class of case, because the work of Longacre and Carter, in Cincinnati, suggests that there may be an actual increase in the size of the lung after pneumonectomy. Doctor Courmand has been studying the pneumonectomies that we have performed on the Children's Surgical Service at Bellevue Hospital during the past three years. The first was performed by Doctor Bohrer, in October, 1937; so we have studies upon patients with pneumonectomies of more than three years' standing, although others are more recent. These studies all show that the children are able to compensate very well for the loss of the lung. Of course, the pneumonectomies were all undertaken for suppurative disease; and the lung was removed intrapleurally. Therefore, they have not had the complete pneumonectomy that is undertaken for carcinoma. However, all the functioning lung has been removed. When these studies have been completed, and the children have been followed for a greater length of time, I believe that we will find there is an actual regeneration of lung; that the remaining lung can take on the function of the lung that was removed; and that these children will be able to grow up without any impairment in their respiratory function.

DR. FRANK B. BERRY (New York) said, in conclusion, that he was particularly grateful for Doctor Lilienthal's discussion. Although the speaker did not mention the various operations—lobectomy *versus* pneumonectomy for carcinoma—he was in agreement with Doctor Neuhoef that some cases do well following lobectomy; he is not completely persuaded that every case of carcinoma should have a pneumonectomy performed, though he may be so convinced at some future time.

Doctor Berry thoroughly agreed with Doctor Eggers that a great deal can be accomplished if patients are seen early. Of the cases shown, at this time, one had had symptoms of the lesion ten months, and the other six months; both happened to be favorable cases. Another patient, whom Doctor Berry thought would be favorable, had had symptoms for more than two years. He developed a very peculiar metastasis recently—apparently a solitary metastasis in his pectoralis major muscle on the operated side, although the tumor was deep in his bronchus, and there was no spilling as the lung was removed. That developed about one year after operation.

As to the patient with the silk ligature: he had a small piece of tumor in the posterior wall of his trachea. He was well until one month ago when he noticed pain in his chest, and is now back in the hospital with empyema, which developed in one of the small pockets of fluid, which is a source of danger in leaving a chest full of organized fibrin and fluid. Some of the pockets, although sterile at the time, are potential foci for later infection. Doctor Berry did not think, however, that this was the whole story with this patient. The patient is beginning to be hoarse and has a wide mediastinum, probably from recurrence of his carcinoma.

MORTALITY FACTORS IN THE SURGICAL TREATMENT OF ULCERATIVE COLITIS

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THREE YEARS AGO, before this Association, one of us (H. W. C.) discussed the surgical treatment of chronic intractable ulcerative colitis, and presented the case histories of six colectomized patients. Radical procedures were advocated as curative measures where irreversible changes had occurred. The series is now considerably larger. We have performed 90 operations upon 50 individuals. There were 11 deaths, a gross mortality of 22 per cent. The 50 cases subjected to surgery were selected from 301 patients seen and studied on the Gray Service of the Roosevelt Hospital during the past five years (Table I).

The wider experience makes it justifiable to enumerate and discuss factors influencing the operative mortality, and to suggest measures which we believe will help in its reduction. The inflammation and ulceration extending deep into the colonic wall, with the secondary pathologic changes in other tissues that characterize this disease, predispose to a high mortality.

It has been difficult to determine, with any degree of accuracy, the incidence of the disease, and difficult to estimate the exact mortality, for no large series has been reported. We have learned from the Bureau of Records, that in New York City, with a population of 7,347,000 individuals, 1,823 died of cancer of the stomach in 1939. In the same year 1,454 died of cancer of the colon, 804 died of cancer of the rectum, while only 59 died of ulcerative colitis.

A comprehensive understanding of the progress of the disease is essential before mortality rates will be lowered. It is a cyclic recurring disease usually divided into four stages: (1) Phase of acute activity. (2) Phase of convalescence. (3) Phase of quiescence. (4) Phase of early recurrence.

The principal indirect mortality factor in the treatment of ulcerative colitis is that surgery comes too late. The thought of permanent ileostomy, with the dread of caring for an almost continuously discharging stoma on the anterior abdominal wall, militates against early surgery; yet, it has to be tolerated, in order that these unfortunate individuals may live.

The physician who sees these patients early must be impressed with the disastrous effects of delay, particularly when the process has reached an irreversible stage. When he has been enlisted to the cause of earlier intervention there will be real hope of diminishing the mortality.

The two major, direct mortality factors are hemorrhage and peritonitis.

Massive hemorrhage in the acute fulminating stage of the disease has been fatal frequently in the past, even before ileostomy could be contemplated as a preliminary procedure. Our experience with ileostomy performed early after massive hemorrhage has proved, for the most part, unsuccessful. We have decided, for this reason, that profuse hemorrhage is no longer an indication for surgery; and recommend risking the outcome with intelligently administered dosages of vitamin K, if the prothrombin is low, and vitamin C, and transfusions. The spasm which predisposes to hemorrhage is relaxed

TABLE I

TOTAL SURGICAL PROCEDURES

TYPE OF PROCEDURE	NUMBER
ILEOSTOMY	34
PARTIAL COLECTOMY	8
SUBTOTAL COLECTOMY	24
ABDOMINO-PERINEAL RESECTION (removal of entire colon and rectum 4)	7
CAECOSTOMY	1
ILEO-SIGMOIDOSTOMY	6
ILEO-TRANSVERSE COLOSTOMY	2
EXPLORATORY CELIOTOMY (including division of adhesions releasing obstruction; volvulus; and attempted removal of rectum.)	6
CLOSURE OF COLOSTOMY	2
TOTAL NUMBER OF SURGICAL PROCEDURES	90
NUMBER OF PATIENTS OPERATED UPON	50
TOTAL NUMBER OF SURGICAL DEATHS	11
GROSS OPERATIVE MORTALITY	22%

with belladonna and papaverine hydrochloride. If this type can be carried conservatively beyond the stage of acute activity with bleeding, into a more chronic form of the disease, fatalities will be avoided.

Ileostomy is not a difficult or formidable procedure, yet it is one attended with a considerable mortality; eight of our 11 deaths followed ileostomy. Of the 34 ileostomies performed, 22 were elective and 12 were undertaken as emergencies.

The 50 per cent mortality (Table II) in the emergency group is high. Three of the six, however, had perforated before operation, and died from the effects of a preexistent peritonitis.

These patients are admittedly poor surgical risks, regardless of whether one classifies them as acute fulminating, with actual or impending perforation; with or without massive hemorrhage; chronically ill, or intractable and debilitated by inadequate and faulty medical management.

The dread of all surgeons interested in colonic surgery is peritonitis; it is the major cause of death in this disease. Nine of the 11 fatalities in our

series were due to this complication. Three of these cases had perforated before operation was undertaken; two seemed unavoidable; and four were due to technical errors on our part which resulted in peritonitis. In these last four cases, one followed embarrassment to the circulation of a loop of

TABLE II

ILEOSTOMY DEATHS

TYPE OF SURGERY	NUMBER OF CASES	DEATHS	MORTALITY
Ileostomies	34	8	23%
Emergency Ileostomies	12	6	50%
Elective Ileostomies	22	2	9%

ileum which was brought out upon the anterior abdominal wall in an effort to increase the safety factor. Two resulted from dropping back what was thought to be a healthy divided stump of the distal segment of the colon; and the fourth was due to soiling while dividing multiple intra-abdominal fistulae at the time of colectomy.

We highly recommend the technical procedure of forming a mucous fistula in the various steps of the operation. The distal divided end of small or large bowel is thus allowed to remain open on the abdominal wall instead of being sutured and replaced into the peritoneal cavity.

During the past year, in an attempt to obviate peritonitis, we have given sulfanilamide orally as a preoperative medication. At operation, we have poured from 6 to 8 Gm. of the crystalline sulfanilamide into the abdominal cavity prior to closure.

The intra-abdominal application of the drug has been performed in some 50 cases of suppurative appendicitis at the Roosevelt Hospital. The dramatic effect against local abscess and spreading peritonitis, as characterized by the lack of a single death from appendicitis during 1940, prompted us to use the drug in this manner.

We have not attempted, as others have done, to take down an ileostomy and establish an anastomosis between the ileum and lower sigmoid, for fear of a resulting peritonitis or spreading of the disease from the questionably healthy sigmoid into the healthy ileum.

There are other factors which play a rôle in diminishing fatalities following surgery. One of the most important is the accurate evaluation of the

patient's true condition, before operative measures are instituted. In our opinion the most difficult problem is to choose the wisest moment for surgery. Impending perforation is unquestionably an indication.

In the chronically ill individuals there are two groups in which we feel justified to advise surgery: (1) Where there is a progressive and continuous extension of the pathologic changes. (2) Where they continue to have char-

TABLE III

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MORTALITY FACTORS

NAME	TYPE OF SURGERY	EMERGENCY OR ELECTIVE	REASON FOR SURGERY	CAUSE OF DEATH
C. D. R.	Ileostomy	Emergency	Perforation before operation	Peritonitis
B. D.	Colectomy	Elective	Intractable	Peritonitis
W. E.	Ileostomy	Elective	Intractable	Embolism
E. H.	Colectomy	Elective	Intractable	Peritonitis
F. G.	Ileostomy	Elective	Intractable	Peritonitis
M. H.	Ileostomy	Emergency	Impending perforation	Peritonitis Hypoproteinemia
F. K.	Ileostomy	Emergency	Fulminating	Peritonitis
J. M.	Colectomy	Elective	Intractable	Peritonitis
J. N.	Ileostomy	Emergency	Hemorrhage Impending perforation	Paralytic ileus
D. R.	Ileostomy	Emergency	Perforation before operation	Peritonitis
G. S.	Ileostomy	Emergency	Perforation before operation	Peritonitis

acteristic periods of recurrence and remission accompanied by an extensive involvement of the colon.

In order to diminish the mortality in the surgical treatment of ulcerative colitis, we cannot emphasize too strongly a meticulous and prolonged medical investigation of these patients. Many abnormal conditions should be corrected before surgery is undertaken. Among them are:

- (1) Active food allergy—the test diet method has proven satisfactory in many instances. These patients do better on a protein diet than on a diet high in carbohydrates, as has hitherto been considered the appropriate “colitis diet.” There has been a variety of foods which have appeared to play a part in the mechanism of this disease; most of these individuals have been allergic to either milk, wheat or eggs. It can be said, with some degree of accuracy, that approximately 50 per cent of the patients indicate that food allergy plays a considerable rôle.

It has been noticeable that no evidence of food sensitization has been demonstrated during the acute stage of the disease, and it has been learned that allergic individuals seem to go through phases of active reactions as well as phases without reaction.

It has been emphasized by Mackie¹ that "all patients suffering from this disease should be repeatedly studied in an effort to demonstrate a food allergy mechanism."

- (2) Disturbed physiology of other parts of the digestive tract should be corrected. Gastric anacidity produces diarrhea and flatulence; hypomotility of the colon with right-sided retention contributes to the degree of pain.
- (3) Functional diets too low in proteins; thiamin chloride; vitamins A, C and D; and certain members of the B complex.
- (4) Anemia should be combated.
- (5) Disturbances of mineral metabolism, including calcium, phosphorus or sodium chloride.
- (6) General malnutrition and inanition.

We believe that adequate and detailed preoperative surgical preparation will assist materially in lowering the mortality. Fluid balance and the blood chemistry can be fairly accurately regulated by daily infusions and transfusions. We know that vitamin C is reduced not only preoperatively but postoperatively. Therefore, these patients are saturated with sufficient vitamin supplements. A nonresidue diet 48 hours prior to the proposed operation helps in keeping the bowel empty, and lead and opium pills and paregoric render the intestine quiescent.

In the earlier group of patients operated upon we used avertin, gas-oxygen-ether as the anesthesia. Lately we have been of the opinion that a spinal anesthesia definitely facilitates the operative maneuver, lessens complications, and is relatively safe. We prefer to use the Howard-Jones solution of nupercaine in 1-1500 dilution with 0.5 per cent saline. To protect these patients against psychic trauma, they are given three nembutal tablets orally two hours before the time of operation, followed in one hour by morphine grains 1/6-1/8 with scopolamine grains 1/150-1/200 hypodermatically. Many of these patients doze throughout the operation and often have little memory of their surgical experience. Fifteen minutes before being brought to the operating room, the patient receives an intramuscular injection of ephedrine, 50 mg., to assist in maintaining the blood pressure.

Spinal puncture is made with the patient in the horizontal position, and the head of the table slightly elevated. The second lumbar space is usually chosen, in order to obtain sufficiently high anesthesia. The dose is varied from 14 to 19 cc., depending on the height and general condition of the patient. Those individuals of short stature, of about five feet three inches, or patients whose resistance has been lowered by the disease receive a smaller dose. The solution is injected slowly. Nupercaine solution is lower in specific

gravity than the spinal fluid, so the patient is immediately turned to the prone position to obtain satisfactory anesthesia of the posterior sensory roots.

An infusion of saline solution or saline and glucose is started at the time that the incision is made. This, we believe, is helpful in preventing any serious fall in blood pressure. Should the patient become restless we have not hesitated in supplementing the spinal anesthesia with inhalations of nitrous oxide. Oxygen inhalations are administered at intervals throughout the operation, particularly if there are signs of nausea, color change, respiratory disturbances or fallen blood pressure.

TABLE IV

SURGICAL MORTALITY

PROCEDURES	NUMBER OF CASES	DEATHS	MORTALITY PERCENTAGE
Ileostomy	34	8	23%
Colectomy			
Subtotal	24	2	8%
Partial	7	1	14%
Ileo-sigmoidostomy	6	0	0
Combined Abdomino-perineal resection	7	0	0

When the disease has involved the entire colon, a three-stage operation, we believe, has proven safest: First, ileostomy; second, subtotal colectomy; third, proctectomy. In the proximal type, where the cecum, ascending and transverse colons are involved, ileosigmoidostomy (end-to-side), with the distal divided end of the ileum brought out as a mucous fistula, has proven eminently satisfactory in our hands.

In that group where the disease has invaded only the rectum and the descending colon, transverse colostomy with the removal of the descending colon as a first-stage, and removal of the rectum as a second-stage, has been successful except in one instance; and that fatality was due to an error in judgment, by attempting to close over the distal divided end of the sigmoid and dropping it back in the peritoneal cavity at the first-stage.

Careful postoperative management, especially following ileostomy, is considered of more vital importance than after the other two stages. In order to insure the immediate functioning of the small bowel through the newly made ileostomy stoma, adequate fluids are administered by venoclysis. The chloride and calcium content of the blood, as well as the serum protein are

checked and an attempt is made to keep up these constituents to a normal level. To maintain the chemical balance, the determination in both plasma and serum is helpful.

Administration of thiamin chloride after operation improves the appetite. These patients are thus more easily coaxed into eating early. In order that the ileal stoma may function almost immediately after operation, we feed them almost immediately after their return from the operation. Chewing gum, melba toast, crackers and cracked ice the day of operation seem to start the ileostomy drainage. A soft, low residue diet in small feedings is given every three hours beginning the afternoon of operation. The second day postoperative, a soft diet with copious amounts of fluids is given; and on the third day, a solid diet is permitted.

Beneficial results of this early feeding are: (1) The ileostomy stoma begins functioning from 12 to 24 hours after operation. (2) There is a minimum amount of postoperative gas and distention, and so the risk of vomiting and ileus is minimized. (3) The weight is maintained, and thus the usual convalescent weight loss is rarely more than three to five pounds.

CONCLUSIONS

Radical surgery has proven justified in the treatment of intractable ulcerative colitis. The primary mortality factor, in our opinion, is that surgery is offered too late. Hemorrhage and peritonitis are dreaded complications of this disease, and those patients who have hemorrhages are best treated by medical management. Let us emphasize the importance of a prolonged and careful medical investigation, and urge that the surgeon see the patient during this time of preoperative medical study.

Ileostomy is associated with a higher mortality than are the other procedures, such as subtotal colectomy and proctectomy.

Oral sulfanilamide, preoperatively, and placed into the peritoneal cavity in the form of crystals at the time of operation has been helpful in reducing the mortality.

The exteriorization of the distal divided end of the small bowel as a mucous fistula after ileostomy is justified as a technical procedure, this also applies to the treatment of the distal divided end of the sigmoid after subtotal colectomy. It is a maneuver that prevents a "blow-out" of the sutured stump, thereby averting peritonitis.

REFERENCE

- ¹ Mackie, T. T.: Jour. Amer. Diet. Assn. **14**, No. 3, March, 1938.

DISCUSSION.—DR. FRANK H. LAHEY (Boston, Mass.): This is one of the subjects, I am very certain, that needs frequent discussion, and is a subject, it seems to me, wherein is well-illustrated the value of the combined efforts of the gastro-enterologist, surgeon and the internist, as is true of thyroid disease. Doctor Cave has associated with him Doctor Mackie, who is also interested in the subject, and, thus, it makes an ideal set-up. It is a dangerous disease because of the limited number of cases occurring in any one man's hands

except those who have a particular interest in it, and the price of acquiring experience is an extremely high mortality. Therefore, it is very desirable that everyone who is dealing with this type of patient, to any great extent, should bring their experience before us.

Doctor Cattell and members of the Gastro-enterologic Department of the clinic, have been much interested in the subject of ulcerative colitis, particularly during the past ten years. Operative treatment has been necessary in a considerable number of these patients, due to complications of the disease, and I should like to present our surgical experience. We have had 280 patients with ulcerative colitis, and in this total group, 80 ileostomies were performed, with a mortality of 20 per cent. Further, in this group of 80 cases, 43 total colectomies, an operation which includes the removal of the rectum, were carried out in stages, with three operative deaths. In addition, 14 partial colectomies were performed without operative mortality when the ulcerative process was segmental or limited to part of the colon. The high operative mortality following ileostomy is due to the fact that this procedure had been delayed too long, and death in these cases is usually due to perforation of the colon. In five patients the ileostomies have been disconnected, restoring the fecal stream, and these patients have remained well. This procedure is justifiable only after a long period of observation following ileostomy, with complete clinical remission of the disease. Furthermore, two additional findings must be present before it is considered: (1) The proctoscopic findings must be negative, showing complete healing of the mucosa; and (2) the barium enema should demonstrate distensibility and contractility of the colon. The fact that the fecal stream can be restored in a few cases without reactivation of the disease makes us feel that early ileostomy is justifiable before extensive damage occurs to the colon.

There are a few points, I think, which should be brought out and stressed. One is that the mortality in ileostomy, as you see in these statistics, is about 20 per cent. This is due to the fact that medical men and patients do not want to face an ileostomy, but we must all strive to see that ileostomies are not undertaken as late as they frequently are. Medical men and gastro-enterologists do not want ileostomies performed, and quite properly so: (1) Because it is such an undesirable type of enterostomy; (2) because they know that the disease is characterized by remissions, and so put it off with the hope that this will occur. When the patient has a high temperature, is prostrated, and everyone—the patient, his family and the medical men—are all convinced that an ileostomy should be made, it is frequently too late. We must perform ileostomies more often at the time when patients do not want them done, if we are to diminish the mortality percentage which goes so often with this procedure, when it is undertaken late.

We have repeatedly said, never perform an ileostomy of the end-type in the acute stage, that is, with the division of the ends; perform, at this time, only the loop-type of ileostomy. This is an emergency, when the patients are extremely ill, with high temperature and intoxication. If you spend the time, then, dividing the ileum and implanting it at two different levels so that later you can perform a colectomy in the stage of the disease which is acute, you will often have a fatality. A fatality at that time will frequently occur because the wall of the bowel is filled with infected organisms, the mesentery with septic thrombi, and the manipulation consequent to cutting the bowel across will cause peritonitis.

There are some rough but practical rules relative to when to perform an ileostomy. Certainly, any patient who has been through two acute episodes

of ulcerative colitis deserves an ileostomy, and it is dangerous to let him go beyond this point. Following an ileostomy many of these patients are greatly improved, but later have recurrence of fever, the discharge of blood and pus, and tenderness over the colon. This is usually due to reactivation of the bowel and blocking-up of its contents due to cicatrization, contractures and strictures. Certainly, any patient who has had two episodes of elevation of temperature, and blood and pus from the colon after an ileostomy deserves consideration of a total colectomy.

There is no more dangerous operation than ileostomy in terms of possible later complications. Often the abdominal wall about the ileostomy is apt to be digested from the effects of the irritating ileal contents. Therefore, it is extremely important to fix the ileostomy to the parietal peritoneum under the edge of the wound, thus guarding against the possibility of a loosening of the ileostomy from the abdominal wall and its retraction into the abdomen.

We do not agree that every patient with a rigid colon is a candidate for ileostomy and colectomy. We have seen at least a few patients with rigid colons who have gotten on, and are getting on, quite well over a long period of time. We believe that one cannot generalize as to this point, but that each case should be dealt with individually.

We need, more than anything else, to get the mortality rate in this disease down by better cooperation between the medical men who see these cases early, and the surgeons who unfortunately now have to operate upon them so late.

DR. HARVEY B. STONE (Baltimore, Md.): I thought it might be of interest to Doctor Cave, and the audience, to tell you that we have tried in a limited number of cases the effect of this new drug, sulfanilyl guanidine, in ulcerative colitis as a therapeutic measure. In these few cases, it is my opinion that it has no value as a curative treatment of the basic disease. One or two of these patients we have been able to follow quite closely. One patient is a member of the Surgical Staff. He had an ileostomy performed about a year ago, and for a number of weeks has had the colon irrigated with sulfanilyl guanidine, and has had repeated proctoscopic examinations made. The mucosa is apparently just as inflamed as before; so that any hope that may have existed as to the curative power of this drug in this disease is not apt to be sustained. I think it will prove very effective as preoperative treatment to cut down the colon group of flora in the bowel and, therefore, to render these dangerous colectomies and ileostomies much less dangerous than they would be without administration of the drug.

There is one other point I would like to mention briefly. I quite agree that if one expects an increased number of patients in whom surgery may lead to a definitive cure of chronic ulcerative colitis, we must perform earlier ileostomies. It is not only the reluctance of the surgeon and the patient to submit to the ileostomy that defers operation, but it is, also, the fact that it is a cyclic disease, and the patient and the doctor constantly live in hope that next week or next month the patient will come out of this stage and go into the quiescent stage—they keep on hoping and defer ileostomy. It seems to me that there is a specific evidence of beginning change in the colon which can be obtained, that is, roentgenographic evidence of increasing rigidity and loss of haustration. When the patient begins to show evidence of change, I think it is likely that he is going into a stage of pathologic development which will not be reversible, and if you expect to establish an ileostomy with the hope of ultimately closing the ileostomy, it must be undertaken early, before irreversible changes occur.

DR. HENRY W. CAVE (New York City, closing): I should like to bring out two or three points; one, is a factor I believe will reduce the mortality—the type of anesthesia. Up to one year ago we employed general anesthesia, but we find now that spinal anesthesia, nupercaine, will give better anesthesia and expedite the operation. We do not like to hurry, and it is not as necessary in most operative procedures as it used to be. But I believe, in taking out the entire colon in desperately sick people, a certain amount of speed will help reduce the mortality. Formerly, we took off the omentum from the transverse colon and let the transverse colon drop more easily. We have abandoned that. We do not think it necessary. Formerly, we did peritonization of the area by removing the colon, and we have abandoned that. We do not think it necessary.

I should like to emphasize Doctor Lahey's statement that we should not be considered mere artisans in doing this; I know of no other disease where close cooperation is more necessary. We have this Ulcerative Clinic, as it is known. Doctor Mackie is there and I see the cases with him. It is sometimes difficult to refrain from operation, but I think the surgeon should be the one to decide and not let the physician pull him into it. Although we have not done it, I think Doctor Lahey's idea of bringing out a loop on the anterior wall, and nothing else, is a good one in the desperately ill patients. I think his classification of when ileostomy and when colectomy should be undertaken is very clear. It is interesting to hear Doctor Stone say that they used sulfanilyl guanidine and had no results. I personally cannot see how any drug can get into the colonic wall and result in any sort of restoration.

To go back to Doctor Lahey's telling of where he has restored the fecal stream by putting it through the colon: I believe in carefully selected patients, where you are sure the rectum and lower sigmoid is somewhat restored, it might be advisable. Doctor Stone, at the American Surgical Association, brought out a very ingenious idea of performing a type of ileostomy with a pocket in it, and I think that should be given consideration. Further, what he says about the early changes in the colon which may be demonstrated roentgenographically, is significant, and then you make your ileostomy and make it early. I did not agree with him last spring, but I am confident that we have had cases in the early stages where they could have been saved had they had ileostomy earlier.

This paper was read before the Fifty-third Annual Session of the Southern Surgical Association, Hot Springs, Va., December 10, 11, 12, 1940.

REGIONAL LYMPHATIC METASTASES OF CARCINOMA OF THE COLON

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A KNOWLEDGE of the incidence and the location of the regional lymphatic metastases from carcinoma primary in the large intestine is essential in the treatment of this disease.

This study, similar to one made by us on the regional lymphatic metastases of the rectum,¹ and the stomach,² is based upon the dissection and examination of all the lymph nodes from 46 cases of carcinoma of the large intestine. This included the following distribution:

TABLE I

Site of Tumor	No. of Cases
Cecum	4
Ascending colon	4
Hepatic flexure	3
Transverse colon	9
Splenic flexure	3
Descending colon	3
Sigmoid colon	20
Total	46

The lymph nodes were dissected from each specimen after they had been visualized (Fig. 1) with clearing by the Spalteholz method, as modified by Gilchrist and David.³ All nodes were examined microscopically and the results charted on a diagram, upon which every node was indicated. The presence or absence of regional lymph node metastases were then correlated with: (1) The age of the patient; (2) sex; (3) duration of symptoms; (4) gross type of neoplasm; (5) size; (6) circumferential extent; (7) depth of infiltration; (8) microscopic type; and (9) the degree of cellular differentiation.

Lymph nodes may be isolated by this method which, because of their smallness, go unnoticed by the usual method of dissection. Many large nodes were found to be inflammatory and many small impalpable nodes were found to contain metastatic carcinoma. Unless a lymph node was definitely replaced by carcinoma, it was impossible to determine without microscopic section whether it was involved. These facts of observation demonstrate clearly that the operative procedure should not be minimized because of the absence of palpable lymph nodes. It is in these cases that cure may be obtained if the operation be radical.

METASTASES OF CANCER OF COLON

As a result of this special method of investigation, 28 of the 46 cases studied, or 60.87 per cent, showed evidence of regional lymph node metastases. An average of 52.07 nodes was isolated per specimen. There was an average of 59.4 nodes isolated per specimen in cases having nodal involvement and 41.4 nodes in those without metastases. Of the carcinomata of the right colon, 62.5 per cent showed metastases in comparison to 60 per cent of those of the left colon.

The superiority of this method of determining the presence of regional lymph node metastases is realized when these findings are compared to those of other workers. Craig and MacCarty,⁴ in 1923, studied the incidence of regional lymph node metastases from 100 cases of carcinoma of the cecum by the usual method of dissection. They were able to isolate only 10.25 nodes per specimen, with an incidence of nodal involvement of 32 per cent. Hayes,⁵ in 1921, found an incidence of 37 per cent nodal metastases in carcinoma of the large intestine, excluding the cecum, in which only 14.06 lymph nodes per specimen were isolated. Rankin and Olson,⁶ in 1933, reported an incidence of 34 per cent regional lymph node metastases in 187 cases of carcinoma of the right colon, and only 31 per cent in 260 cases of carcinoma of the left colon.

In 1939, Simpson and Mayo⁷ reported an incidence of 41.4 per cent nodal metastases in 120 patients with carcinoma of the colon. These were distributed as follows:

TABLE II

Site of Tumor	No. of Cases	No. of Cases with Metastases	Percentage
Right colon.....	28	14	50.0%
Transverse colon.....	15	6	40.0%
Descending colon.....	26	12	46.2%
Sigmoid colon.....	51	15	29.4%
Totals.....	120	47	Avg. 41.4%

The incidence of nodal metastases and the anatomic distribution of our cases are:

TABLE III

Site of Tumor	No. of Cases	No. of Cases with Metastases	Percentage
Cecum.....	4	3	75 %
Ascending colon.....	4	2	50 %
Hepatic flexure.....	3	1	33.3%
Transverse colon.....	9	7	77.7%
Splenic flexure.....	3	2	66.6%
Descending colon.....	3	2	66.6%
Sigmoid colon.....	20	11	55.0%
Totals.....	46	28	Avg. 60.87%

It is interesting to note that there were three patients with well-differentiated papilliferous adenocarcinomata of only Grade II malignancy, who had small hepatic metastases without demonstrable local regional lymph node involvement.

Regional lymph node metastases is only one factor in determining the operability and prognosis of carcinoma of the large intestine. Inoperability or poor prognosis may result from extensive local infiltration, hematogenous metastases or peritoneal implants. Ten per cent of the neoplasms (five of 46 cases) showed microscopic evidence of infiltration into blood vessels. This figure is slightly less than the incidence of 15 per cent microscopic infiltration of blood vessels noted by us in both carcinomata of the rectum and stomach. These were, in early cases, suitable for operation prior to demonstrable gross

hematogenous metastases. As to local infiltration, 93.1 per cent had completely infiltrated through the bowel wall. This is a constant source of free peritoneal implantation.

Lymphatic Drainage of the Large Intestine.—Delamere, Poirier and Cuneo,⁸ and Jamieson and Dobson⁹ were the first thoroughly to investigate the lymphatic drainage of the large intestine. This consists of three systems: The intramural; intermediary; and extramural lymphatic networks.

The intramural system consists of the submucosal, intermuscular and subserosal networks. Where the large intestine is devoid of a continuous longitudinal muscle layer, the intermuscular and subserosal networks are the same. The lymph channels



FIG. 1.—Photographs of cleared specimens of carcinoma of the rectum.

begin about the mucosal glands of Lieberkühn and drain to the submucosal network. This network communicates freely with similar channels above and below the site of the lesion, but lymph tends to flow toward the deeper intermuscular and subserosal networks. Since lymph channels follow the course of the radial blood vessels around the circumference of the bowel, carcinomata of the large intestine, as well as the rectum tend to be annular. The lymph then flows from the intramuscular system through the intermediary lymph channels to the extramural lymphatic system. This consists of a group of nodes and lymph channels anatomically arranged about the blood vessels and are described by Jamieson and Dobson⁹ as corresponding to these vessels. Thus, there is the ileocolic chain; the right colic chain; the middle colic chain; the left colic chain; and the inferior mesenteric chain. Along each chain, there are aggregations of nodes that are designated as the epicolic, paracolic, intermediate, and the main group of nodes.

The epicolic nodes lie anterior or posterior to the intestinal wall. The paracolic nodes are located upon the medial aspect of the intestine along the vascular arcades and the short terminal vessels leading from the arcades. The intermediate nodes are situated about midway between the arcades and

METASTASES OF CANCER OF COLON

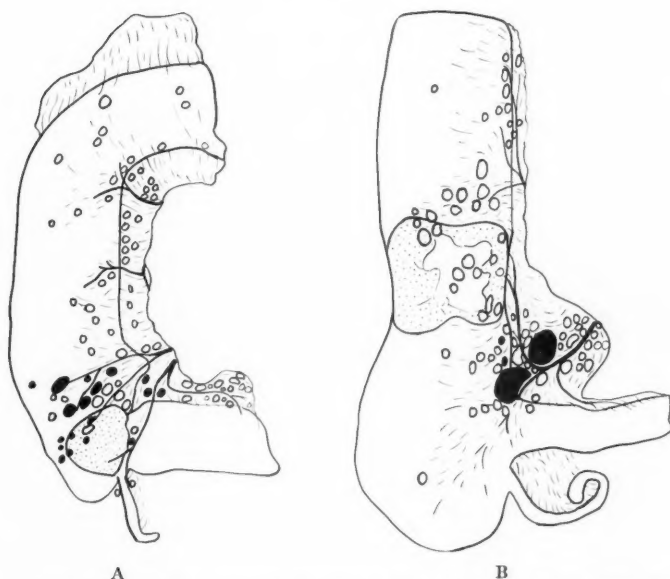


FIG. 2.—(A) Line drawing illustrating the regional lymphatic metastases along the ileocolic chain from carcinoma of the cecum. (B) Line drawing illustrating the downward spread of lymphatic metastases to the ileocolic chain from carcinoma of the ascending colon.

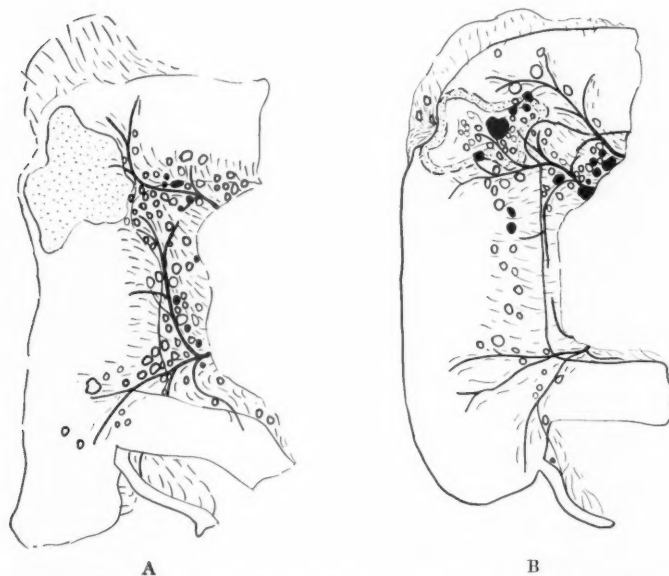


FIG. 3.—(A) Line drawing illustrating two routes of lymphatic metastases from carcinoma of the hepatic flexure; one downward along the ileocolic chain, the other along the middle colic chain. (B) Line drawing illustrating two routes of lymphatic metastases from carcinoma of the hepatic flexure; one along the right colic chain, the other along the middle colic chain.

the origins of the ileocolic, colic, or sigmoidal branches, whereas the main group surrounds the stems of the vessels at their origins.

The ileocolic route of spread drains the terminal ileum, cecum, appendix and the greater part of the ascending colon. Figure 2 A aptly demonstrates this route of lymph node metastases from carcinoma of the cecum. In Figure 2 B, a carcinoma of the ascending colon, the downward metastases toward the ileocecal junction is well shown.

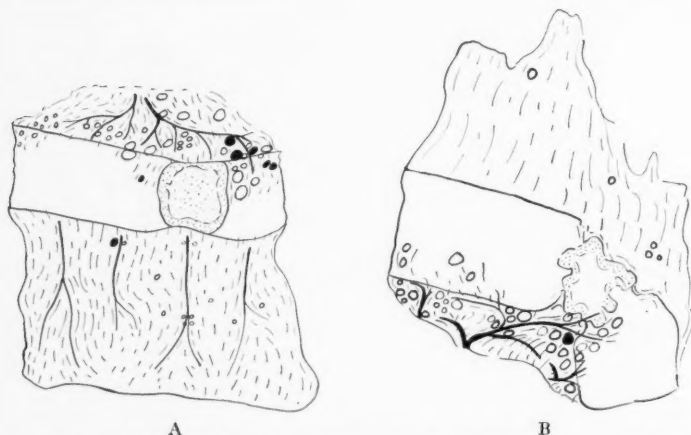


FIG. 4.—(A) Line drawing illustrating the regional lymphatic spread along the middle colic chain from carcinoma of the transverse colon and, also, the metastases of carcinoma of the transverse colon to lymph nodes in the omentum. (B) Line drawing illustrating the regional lymphatic metastases from carcinoma of the splenic flexure.

The right colic chain drains the area supplied by the right colic artery. These nodes are not constant, in that the right colic artery is not constant. They may drain downward into the ileocolic chain, may go medially toward the superior mesenteric nodes, or may drain upward into the middle colic chain. Figure 3 A, demonstrating the lymph node metastases of a carcinoma of the hepatic flexure, illustrates two routes of spread, one downward along the ileocolic chain, and the other passing more medially along the middle colic chain. Whereas, in Figure 3 B the carcinoma of the hepatic flexure appears to be metastasizing by the right colic chain, as well as the middle colic chain, to a lesser extent.

Similarly, the middle colic chain drains the area of distribution of the middle colic artery; that is, the upper part of the ascending colon, hepatic flexure and the proximal two-thirds of the transverse colon. Since the direction of the middle colic artery is to the right, toward the head of the pancreas, in the base of the mesocolon, the spread of metastases is downward and then toward the right. Furthermore, there is a communication between the lymphatics of the transverse colon and those of the omentum, which drain into the nodes along the greater curvature of the stomach. Figure 4 A illustrates this point.

The left colic chain drains the area of distribution of the left colic artery (Fig. 4 B). Neoplasms of the distal one-third to one-half of the transverse

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colon would tend to drain toward the left, whereas neoplasms of the upper descending colon might drain either upward toward the splenic flexure (Fig. 5 A), or downward toward the sigmoidal vessels (Figs. 5 and 6). Lesions of the splenic flexure may spread through lymphatics of the omentum and eventually drain to the splenic lymph nodes.

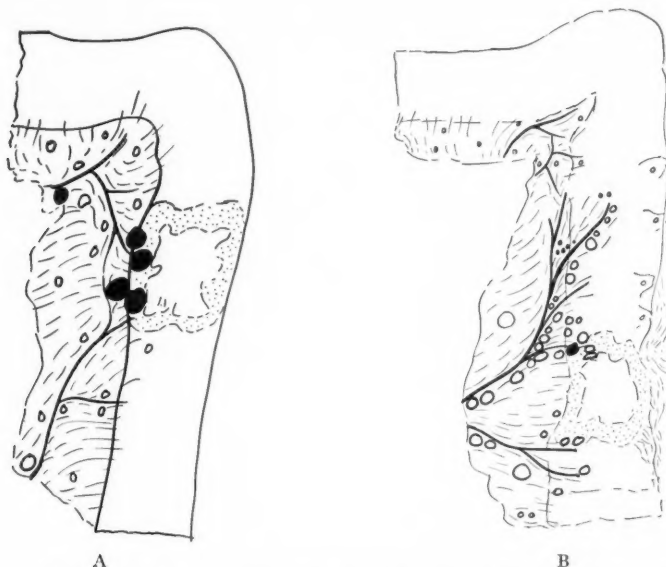


FIG. 5.—(A) Line drawing illustrating the upward lymphatic metastasis of carcinoma of the descending colon along the left colic chain. (B) Line drawing illustrating the regional lymphatic metastasis of carcinoma of the descending colon along the sigmoidal chain.

The inferior mesenteric chain, and specifically the sigmoidal division, drains the area of distribution of the sigmoid vessels. Here, the intermediate nodes lie along the sigmoidal vessels, while the main nodes lie along the course of the inferior mesenteric vessels. Figures 6 A and 7 show, diagrammatically, the lymph spread of carcinoma of the sigmoid colon, demonstrating metastases to the epicolic, paracolic, and intermediate lymph nodes while a single paracolic metastasis is seen in Figure 6 B.

Since it is impossible to determine the presence or absence of regional lymph node metastasis by manual palpation, and since this study has shown that 60.87 per cent of the neoplasms of the large intestine have metastasized to lymph nodes, the surgeon must recognize the necessity of including these areas within the confines of the operative resection, even in the absence of palpable nodes.

Lymphatic vessels differ from blood vessels in that instead of one or two channels draining the same area, the lymph is returned by a number of channels which tend to form a plexus about the blood vessels. There may also be a number of efferent vessels to any one node, thus explaining the observation that contiguous lymph nodes may not be involved. As a rule, the epicolic nodes are the first to be involved by metastatic neoplastic emboli. However,

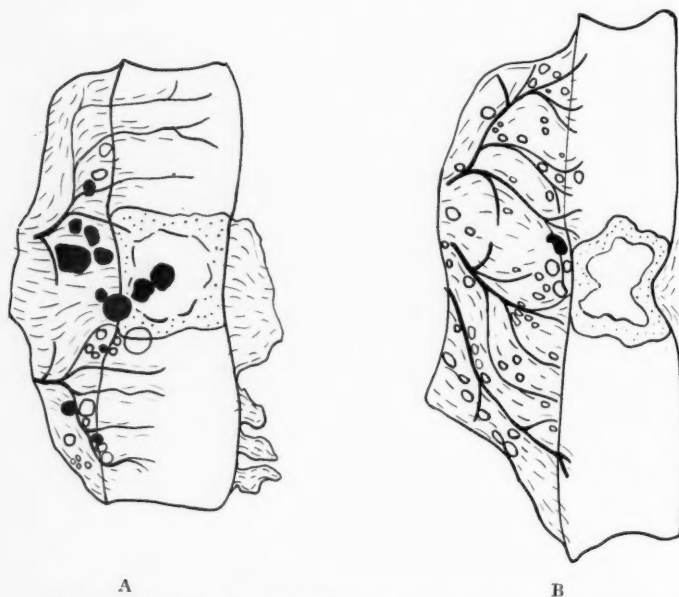


FIG. 6.—(A) Line drawing illustrating regional lymph node metastases to the epicolic, paracolic and intermediate lymph nodes of the sigmoidal chain from carcinoma of the sigmoid colon. (B) Line drawing illustrating the singular regional paracolic metastasis from carcinoma of the sigmoid colon.

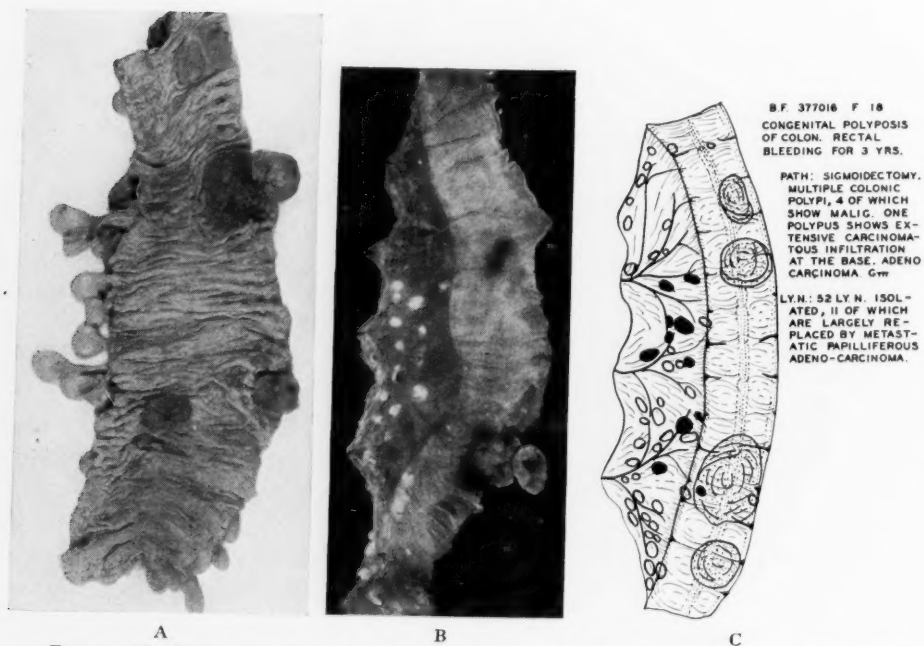


FIG. 7.—(A) Photograph of gross specimen of sigmoid colon illustrating polyposis of the colon in which four of the polyps had undergone malignant proliferation. (B) Photograph of cleared specimen shown in Figure 7 A. (C) Line drawing illustrating the regional lymph node metastases from carcinoma of sigmoid colon demonstrated in Figure 7 A.

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often the neoplastic embolus is contained within a lymph channel that drains directly to either the paracolic or intermediate nodes without primary epicolic lymph node involvement. Lymph nodes act as barriers to filter out neoplastic emboli. A neoplastic embolus enters a lymph node by its peri- and subcapsular lymph channels. If the metastasis remains viable, it sets up a new neoplastic focus, tending to block the lymph channel, which then becomes dilated and

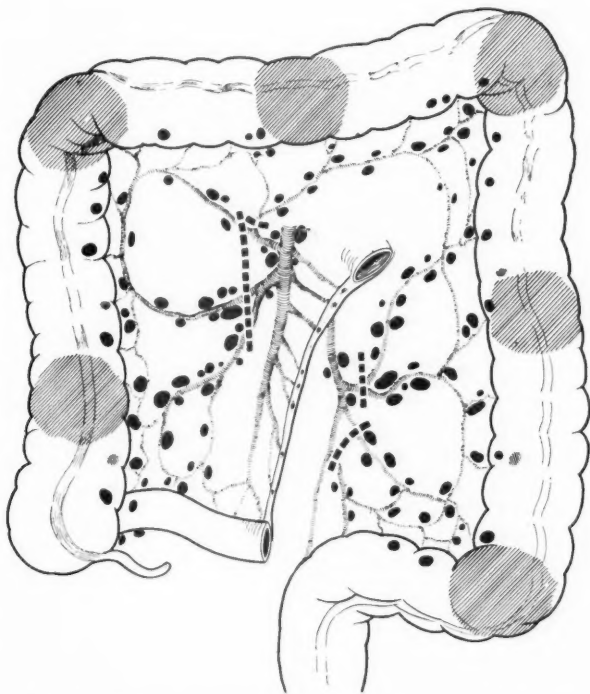


FIG. 8.—Diagrammatic drawing illustrating the lymphatic metastases from carcinoma of the colon. The dotted lines represent the ideal lines of section of the mesocolon to include the possible epicolic, paracolic, and intermediate lymph node metastases.

distended with lymphocytes. Lymph flow becomes static and other neoplastic foci are often established along the course of the lymph channels. The direction of lymph flow determines the direction of lymphatic metastases. If the lymph channels become plugged with neoplastic emboli, then the lymph will find unobstructed channels and neoplastic emboli may metastasize along other zones of spread.

Figure 8 summarizes, diagrammatically, the lymphatic drainage of the large intestine. The surgeon should include within the confines of the resection not only the primary growth but also its epicolic, paracolic and intermediate nodes of lymph drainage. If the carcinoma has metastasized to the main group of lymph nodes at the origins of the various vessels, then generalized metastases, undoubtedly, have already occurred, and any operative procedure would only be palliative in character. In Figure 8, the dotted lines represent the ideal

lines of section of the mesocolon for the various sites of carcinoma of the large intestine and simply restate the original suggestions of Jamieson and Dobson.⁹

Age and Metastases.—The average age of patients with metastases was 50.9 years, in comparison to 59.1 years in those without. There were two cases 18 years of age, a brother and sister, both of whom had polyposis of the colon, with multiple areas of carcinomatous proliferation (Fig. 7). Although these carcinomata were graded II and III, there was evidence of early hepatic metastases at the time of operation. Since both patients were obstructed, resections were performed, and the bowel continuity restored. The third youngest patient, a male, age 27, also had lymph node metastases. There were eight patients 67 years of age or over, five of whom (62.5 per cent) had metastases. Seventy-five per cent of the patients (nine of 12 cases), 50 years of age or below, had metastasized, in comparison to 55.8 per cent of the patients (19 of 34 cases) above 50 years of age. This substantiates the view that prognosis is less favorable in the younger age-groups than the older.

Sex and Metastases.—There was no essential difference between sex and the presence of lymph node metastases. Sixty-one point nine per cent of the male patients (13 of 21 cases) had nodal involvement, in comparison to 60 per cent (15 of 25 cases) of the female patients.

Duration and Metastases.—It was noted that the patient with a short duration of symptoms did not always have as favorable a prognosis as the patient who had had symptoms for a longer period of time. In the groups, as a whole, there was an average duration of 10.4 months in patients having regional lymph node metastases, as compared to an average of 11.5 months in those without. In analyzing the data further, there was an incidence of only 40 per cent metastases (four of ten cases) in patients who had had symptoms for two years or more, in contrast to an incidence of 73 per cent metastases (eight of 11 cases) in patients with symptoms of three months or less. This emphasizes the fact that many patients with symptoms of long duration and who are still operable often have the best prognosis, in that the neoplasm is slowly growing and of low malignancy. These apparent discrepancies are explained by the fact that only lesions that were resected could be studied and all inoperable lesions are thus, automatically, excluded from the study.

Gross Types and Metastases.—The carcinomata of the large intestine were classified into two groups, the polypoid and the sessile. The classification was based entirely upon whether the neoplasms tended to be bulky and to grow out into the lumen (polypoid) or whether they were plaque-like and tended to infiltrate—to be invasive (sessile). The other gross characteristics, such as stenosing, annular, constricting, and ulcerating, we did not feel to be of any clinical value in determining prognosis or likelihood of metastases. It is frequently stated that carcinomata of the right half of the colon are large, ulcerating, fungating, polypoid carcinomata and that those of the left colon are small, annular, stenosing, scirrhus carcinomata. Differences in the gross characteristics of these neoplasms are not the result of any inherent factor within the neoplasm itself to assume these forms, but rather are the result of

the location in which they are found. The caliber of the right colon is considerably larger than that of the left colon, consequently a neoplasm will have acquired a larger size in the right colon than the left before symptoms referable to its presence are made known. There were as many polypoid carcinomata of the left colon as of the right colon, and in all cases there was evidence of ulceration. Twenty of the 13 carcinomata of the sigmoid flexure were stenosing in character—one in the ascending colon, two in the hepatic flexure, four in the transverse colon, three in the splenic flexure, and three in the descending colon. None of these carcinomata was shown, microscopically, to be scirrhus in character. As to the correlation between gross type and regional lymph node metastases, 57.5 per cent of the polypoid neoplasms (23 of 40 cases) had metastasized, in comparison to 83.3 per cent of the sessile neoplasms (five of six cases), demonstrating the more benign character of the polypoid growths.

Size and Metastases.—It has been mentioned that the group with metastases had given symptoms a shorter time than those without. It is of interest to note that the incidence of metastases is higher in the smaller lesions than in the larger. In order to arrive at a more accurate figure as to the size of the neoplasm, its area rather than any one diameter was used. The average size of carcinomata of the right colon with metastases was 32.75 sq. cm., in comparison to those without metastases, in which the neoplasms averaged 39.5 sq. cm. Similarly, the average size of neoplasms of the left colon with metastases was 22.11 sq. cm., in comparison to 31.73 sq. cm. in those without metastases. Thus, we see that the neoplasms in which nodal involvement occurred were definitely smaller than those in which there were none, indicating that the smaller neoplasms giving rise to symptoms were more malignant in character and metastasized sooner. Furthermore, it is noted that the neoplasms of the right colon are considerably larger than those of the left. The largest neoplasms of the entire group were those located in the cecum; these averaged 46.56 sq. cm. in size—accountable by the fact that the caliber of the lumen of the cecum is the largest in size.

Circumference Involved and Metastases.—In no case was there less than 25 per cent of the circumference involved. The majority of the neoplasms (37 of 46) were completely annular. In only three instances had the carcinomata involved less than 50 per cent of the lumen and, in three cases, had involved less than 75 per cent of the lumen. The remaining three cases were included in the group having from 75 to 100 per cent circumferential involvement. Because of the large incidence of completely annular carcinomata, the correlation between circumferential involvement and metastases is not striking. It is noted, however, that of the three cases in which between 25 to 50 per cent of the circumference was involved, only one had metastasized.

Depth of Infiltration and Metastases.—As might be expected from these observations, in which 40 of the 46 carcinomata were either completely annular or found to involve over 75 per cent of the bowel circumference, and had also attained large size before symptoms were produced, in all but three cases the neoplasm had completely infiltrated through the bowel wall. Of the three

infiltrating only partially through the musculature, two had already metastasized. Consequently, any attempt at correlation of depth of infiltration and the presence of lymph node metastases is futile.

Degree of Cellular Differentiation and Metastases.—The preponderance of the carcinomata were graded II as to cellular differentiation. This included 36 of the 46 patients. There were nine neoplasms graded III, and only one graded IV. There were no Grade I carcinomata in our series. As shown in Table IV, the incidence of lymph node metastases was directly proportional to the degree of cellular differentiation.

TABLE IV
DEGREE OF CELLULAR DIFFERENTIATION AND METASTASES

Grade	No. of Cases	No. with Metastases	Percentage
II.....	36	21	58.3%
III.....	9	6	66.6%
IV.....	1	1	100%
Totals.....	46	28	

Microscopic Type and Metastases.—The majority of the carcinomata were found, histologically, to be simple adenocarcinomata. These composed 29 of the 46 cases. The papilliferous adenocarcinomata had the smallest incidence of nodal involvement. These metastasized in only 37 per cent of the cases. The medullary adenocarcinomata had the highest incidence of metastases, and metastasized in 80 per cent of the cases. The second highest incidence was noted in the adenocarcinoma mucosum. Table V designates the number and incidence of the various histologic types with metastases.

TABLE V
HISTOLOGIC TYPE AND METASTASES

Histologic Type	No. of Cases	No. with Metastases	Percentage
Papilliferous adenocarcinoma.....	8	3	37.5%
Adenocarcinoma (simplex).....	29	18	62.07%
Adenocarcinoma mucosum.....	4	3	75.0%
Medullary adenocarcinoma.....	5	4	80.0%
Totals.....	46	28	

SUMMARY AND CONCLUSIONS

A study of the lymph nodes in 46 specimens of carcinoma of the colon was made by David and Gilchrist's modification of the method of Spalteholz. An average of 52 nodes were isolated per specimen. These were examined microscopically and charted on diagrams. Sixty point eighty-seven per cent of the specimens showed evidence of involvement of the lymph nodes by metastases. There was an average of 59.4 nodes isolated per specimen in those showing nodal involvement, and 41.4 nodes isolated in specimens showing no metastases. Sixty-two point five per cent of carcinomata of the right colon showed metastases, in comparison to 60 per cent of those of the left colon.

The routes of spread of carcinoma by the lymph channels are discussed.

Size of nodes is not an index of metastatic involvement. Duration of disease and size of tumor are not correlative with extent of nodal involvement.

Operation for removal of carcinoma of the colon should be planned on an anatomic basis, so as to include lymph node-bearing areas rather than on palpability of lymph nodes. The presence of metastases in lymph nodes from carcinoma of the colon is more frequent than indicated by previous studies based on isolation of lymph nodes by gross methods of dissection.

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RECURRENT CARCINOMA OF THE RECTUM

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Case Report.—In November, 1924, a male, age 26, was referred to the Johnston-Willis Hospital for study. Two years ago, in 1922, the patient had first noticed blood on defecation. For about a year thereafter his condition showed little change; but, in 1923, he began to feel that there was some obstruction low down in his abdomen, and that his bowel movements were incomplete. Occasional laxatives failed to relieve him. He resorted to enemata about three times a week, which afforded temporary relief. He became nervous, but slept well; had an excellent appetite, no nausea or vomiting, and no abdominal pains except when enemata were not employed. He had lost about ten pounds during the past year.

He consulted his family physician early in the fall of 1924, complaining only of the rectal bleeding and the constipation, which had increased over the past 15 months.

This patient's family history was significant. A brother died of carcinoma of the stomach at age 27; his grandfather died of carcinoma of the rectum. In 1919, the patient had an infected ulcer on his leg which lasted six weeks. No specific treatment was administered.

Laboratory Data.—Repeated Wassermanns were negative; spinal fluid, negative; hemoglobin, 68 per cent.

A barium enema showed an annular filling defect in the rectum, within seven centimeters of the anus. The defect itself was about three centimeters long, and the caliber of the rectum was obliterated to a diameter not much larger than that of a lead pencil.

Complementing the roentgenologist's report, the findings of digital and proctoscopic examinations converged on a diagnosis of carcinoma of the rectum. The diagnosis was confirmed by biopsy.

On November 21, 1924, a Kraske resection of the rectum was performed. The dissection was extended into the peritoneum. The peritoneal cavity was opened anteriorly, and the entire rectum with adjacent nodes was removed. The growth was reported to be a carcinoma Grade II, with involvement of adjacent nodes (Fig. 1).

The patient was discharged from the hospital six weeks after operation. Because of his age, only 26, and the malignant involvement of his nodes, I kept in touch with this case for a number of years. His functional results were reasonably good. He continued in business as a successful architect, was married in 1928, and has a daughter now nine years old.

In November last year, he was referred to me again for treatment of what his surgeon thought to be a liberal redundancy about the stoma. A local examination and biopsy proved this to be a carcinoma of much the same type as previously reported. After the necessary preparations, the patient was operated upon again, December 11, 1930. A combined abdominal and posterior resection was completed in one stage. Some difficulty was encountered because of scar tissue from the former operation. However, the patient stood the operation well.

A troublesome ileus developed during the convalescence, but use of our weighted Miller-Abbott tube saved him from an enterostomy, and enabled the patient to make a complete operative recovery.

This time, the pathologic report showed that both the growth and the nodes were adenocarcinoma, Grade III.

Certainly, the above case report presents nothing original or new in symptoms or surgery. The symptoms are classic, the treatment standard. Instead

CARCINOMA OF RECTUM

of the former operation carried out for resection of the rectum, a combined abdominoperineal resection, for a good surgical risk, would be our choice to-day. The writer feels, however, that an abdominoperineal resection in 1924 would hardly have changed the outcome in this case. Our real interest lies

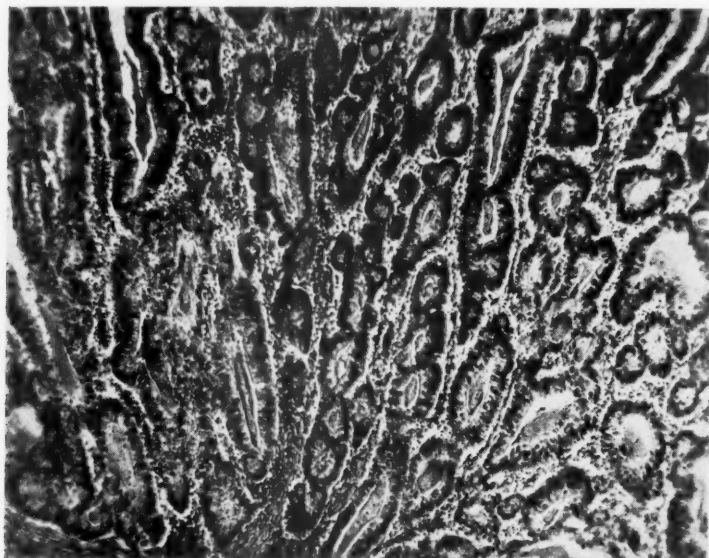


FIG. 1.—Photomicrograph of tumor removed November 21, 1924. Diagnosis: Adenocarcinoma of rectum—Grade II.

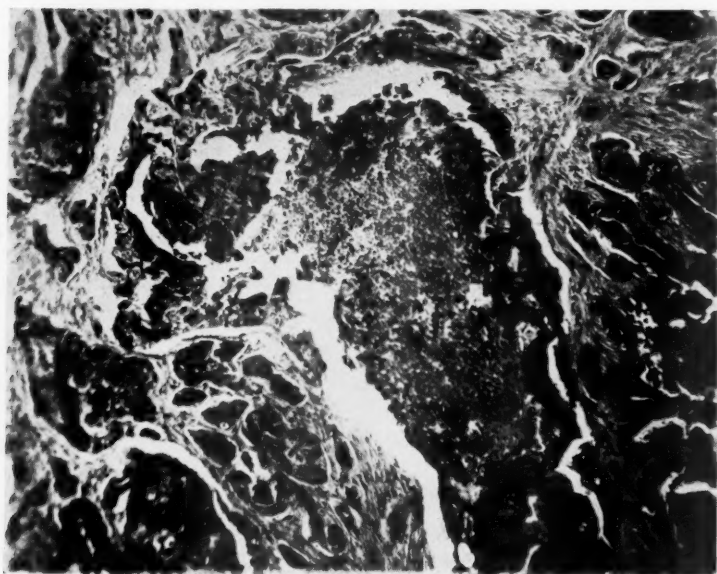


FIG. 2.—Photomicrograph (low power) of the recurrent tumor. Removed December 11, 1939. Diagnosis: Adenocarcinoma of rectum—Grade III.

in the fact that so young a man remained active and well for more than 15 years after the removal of a carcinoma Grade II with lymph node involvement; but was then found to have an operable recurrence of a similar type of adenocarcinoma with the same lymph node involvement. Although more

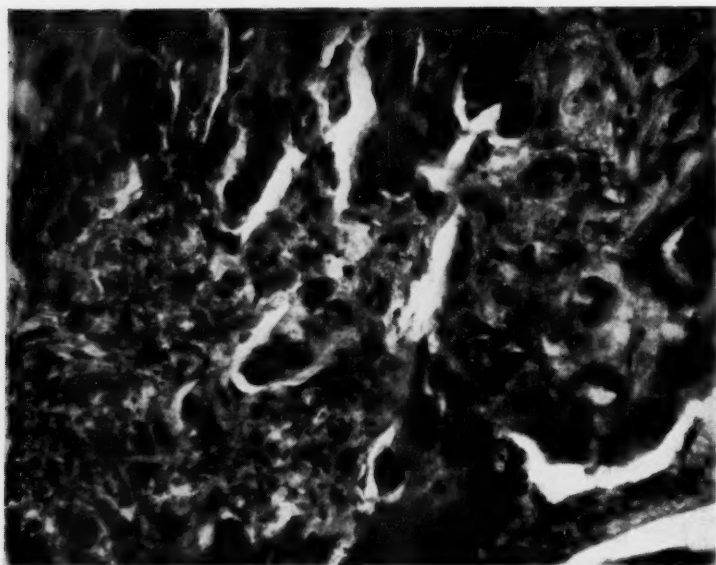


FIG. 3.—Photomicrograph (high power) of Figure 2, showing hyperchromatic nuclei with an abundant cytoplasm, and mitotic figures.

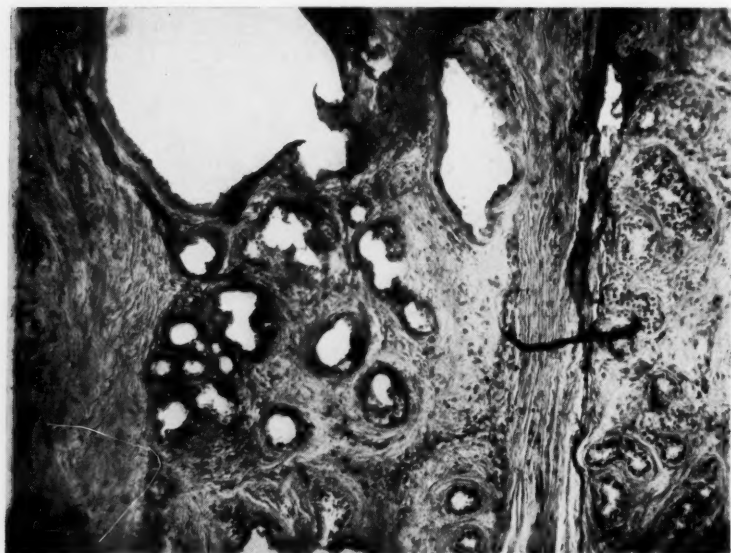


FIG. 4.—Photomicrograph (low power) showing normal and abnormal sweat glands.

than 15 years had elapsed since his primary malignancy, we have classed this case as "a recurrence." At his second operation, the patient presented nearly the same type of lesion; the pathologist reported "a striking resemblance in the cell morphology to the previous growth, and that this was probably of similar cell origin."

Not much parallel is to be read, or information had, on this condition. References to operable "recurrence" are scant in cancer literature. Jerome M. Lynch¹ in an interesting case-report says: "I operated upon Mrs. G. in 1926, performing a combined abdominoperineal operation with a perineal stoma. I excised 25 cm. of the lower bowel, including the anus. The growth (Broders Grade II) was found to begin 4 cm. above the anal verge, and to extend 5 cm.

"There was also a chronic inflammation of the lymph nodes. Two years later, there was a recurrence of the disease. It consisted of two separate growths, both of which were Grade III, more malignant than the primary lesion. I must say that it was with some misgivings that I undertook to operate a second time. Seven years have elapsed since the second operation, and the family tells me she is the most cheerful person in the neighborhood and one of the most active."

In Lynch's case, it should be noted that the lymph nodes were inflammatory, not malignant. But within two years there was a recurrence of the carcinoma. It is also notable that this patient had remained well for seven years after her second operation for cancer.

Richard B. Cattel states that in the presence of a recurrence, roentgen ray and radium therapy definitely increase the duration of life and contribute to the patient's comfort. He makes no reference to further surgery. From this and other reports in the literature, the accepted treatment for recurrence in carcinoma is not surgical. The preponderance of evidence is in favor of radium and roentgenotherapy.

We fully realized, at our patient's first operation, that a 26-year-old man, with gross symptoms of more than two years' duration, stood a good chance for a cancer recurrence. We were especially concerned after the lymph nodes about the rectum were found to be of the same grade malignancy. At the end of five years he reported for examination. A thorough check-up failed to show any irregularity. He was married, had one child, was successful in business, and enjoying good health. Ten years passed, and he reported continuing good health. When he reported himself well after 15 years, we really discharged him as a "cancer cure."

We learned, during the sixteenth year of his recovery, that he was having trouble again, but we supposed, of course, that it would be from an irritated, redundant perineal stoma. However, on his arrival for examination, we realized at once that he had a local recurrence of carcinoma of the stoma. Upon further examination we found that, this time, the growth extended about 7 cm. above the stoma.

After removing this growth, we were impressed to learn that the path-

ology from the bowel and lymph nodes were strikingly similar to that from the former operation, except that these were found slightly more malignant than the tissues removed 15 years previously.

One year has now elapsed since our second operation upon this case of recurrent carcinoma of the rectum. He has been active again in his business; and on examination a few days ago, he seemed to be in good health. But our experience with this patient somewhat dampens any attempt to declare a cure in the case of cancer.

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This paper was read before the Fifty-third Annual Session of the Southern Surgical Association, Hot Springs, Va., December 10, 11, 12, 1940.

RESULTS WITH THE FASCIA PLASTIC OPERATION FOR ANAL INCONTINENCE

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ABOUT 12 YEARS AGO, one of the present writers¹ presented to the Southern Surgical Association a method for restoration of control of the anal outlet, which was based upon an original idea of the Russian orthopedic surgeon, R. R. Wreden.² A few years later, he published two other papers,^{3, 4} relating further experience, and modifying somewhat the technic of the operation. Since then there has been no change in the essential technic, but considerable additional experience with its employment has accumulated, and, also, time has permitted a study of the late results. It seemed to us that a report of such a study would provide a basis for estimating the value of the operation.

A brief résumé of the operative steps is perhaps indicated: With the patient in the lithotomy position, the usual surgical clean-up is carried out. This will be much more effective, and the operative success made more probable if the patient has been prepared for several days previously with a low residue diet and daily measures to empty and cleanse the colon.

Two small incisions are placed symmetrically on either side, parallel to the line joining the tip of the coccyx to the tuberosity of the ischium, and about 2 cm. posterior to the anal margin. These wounds are deepened bluntly into the subcutaneous fat. Then, by blunt dissection a curved Kelly clamp is pushed from one incision to the other, in front of the rectum, in the subcutaneous fat, care being taken to avoid injury to the rectum, anal canal, or vagina. The clamp is then opened and is made to grasp and lock on the ends of two strips of fascia at least 12 to 15 cm. long and about 0.5 cm. wide. This fascia may be either autogenous from the patient's thigh, or prepared sterile ox fascia. We think one gives as good results as the other in this particular operation, and, hence, usually employ the more easily obtainable ox fascia. The clamp holding the strips of fascia is now pulled back through the tunnel that it has made, which thus places two fascia strips in front of the anal canal, in the subcutaneous tissues. A Kelly clamp then is pushed, in similar fashion, from one incision to the other in the subcutaneous tissue behind the anus, and carries with it the end of one of the fascia strips from the first incision to the second. This end is drawn out of the second incision, so that this strip enters one incision, encircles the anus under the skin and emerges from the same incision. Before the clamp is drawn back, it grasps the end of the other strip. It is then withdrawn, pulling this second strip with it. Thus, the second strip also encircles the anus, but from the opposite side and its two ends emerge from the opposite incision. The finger is then inserted into one of the incisions and feels outward and backward until the mesial

margin of the gluteus maximus is defined. An aneurysm needle or clamp carrying a strong guide thread is then pushed around a substantial bundle of the gluteus muscle. This thread is tied to one of the ends of fascia lying in the incision, which is then pulled around the bundle of gluteus fibers.

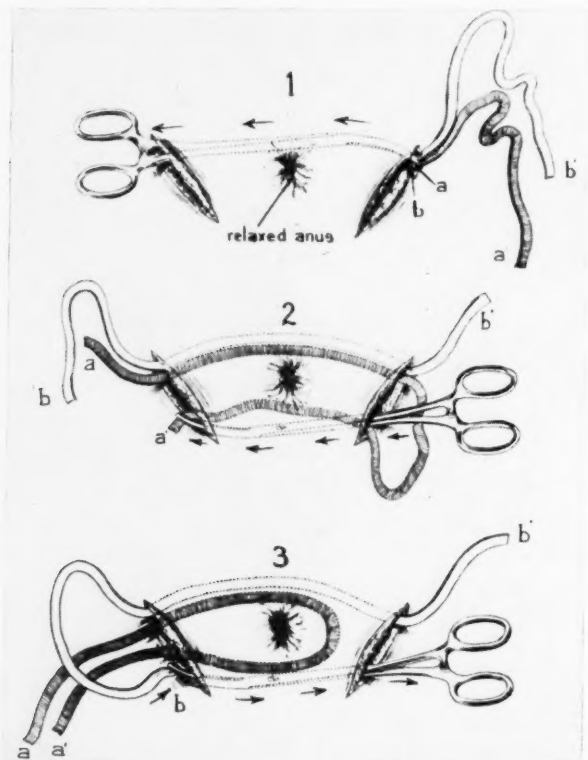


FIG. 1.—Steps in the plastic operation for anal incontinence: (1) Clamps are passed subcutaneously in front of the anus grasping the strips of fascia and are about to be pulled from one side to the other. (2) Both strips are passed subcutaneously in front of the anus and one posteriorly. (3) The loops of fascia encircle the anus subcutaneously in opposite directions. (Arch. Surg., 24, 123, 1932)

This end of the strip is then tied to the other end of the same fascia strip, in a firm square knot, with enough tension to close the anal opening snugly, but not with strangulating tightness. A similar maneuver is carried out on the other side. Thus, the two fascia strips form closed rings which encircle the anal canal on their inner or mesial curves, and a bundle of gluteus fibers on their outer curves, but pull against each other and firmly close the anal canal. These steps are shown in Figures 1, 2 and 3.

Thirty cases, operated upon by six surgeons, have been reviewed. The data concerning these cases were derived from the records of the Johns Hopkins Hospital, the Union Memorial Hospital, and the Church Home and Infirmary.

It is worth while to note that all of these patients suffered from a degree of incontinence severe enough to cause them to seek surgical treatment for its

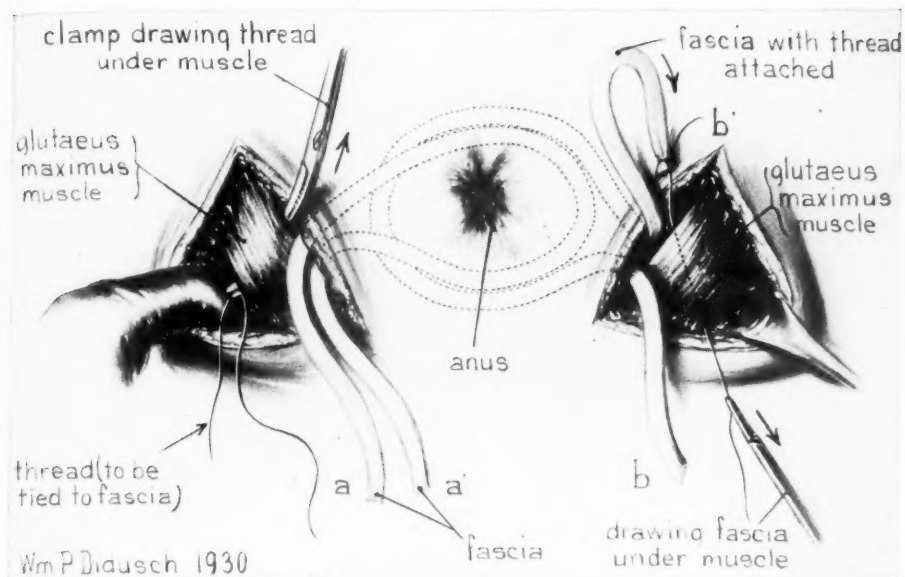


FIG. 2.—The outer ends of the strips of fascia are passed around the bundles of the gluteus muscle. (Arch. Surg., 24, 124, 1932)

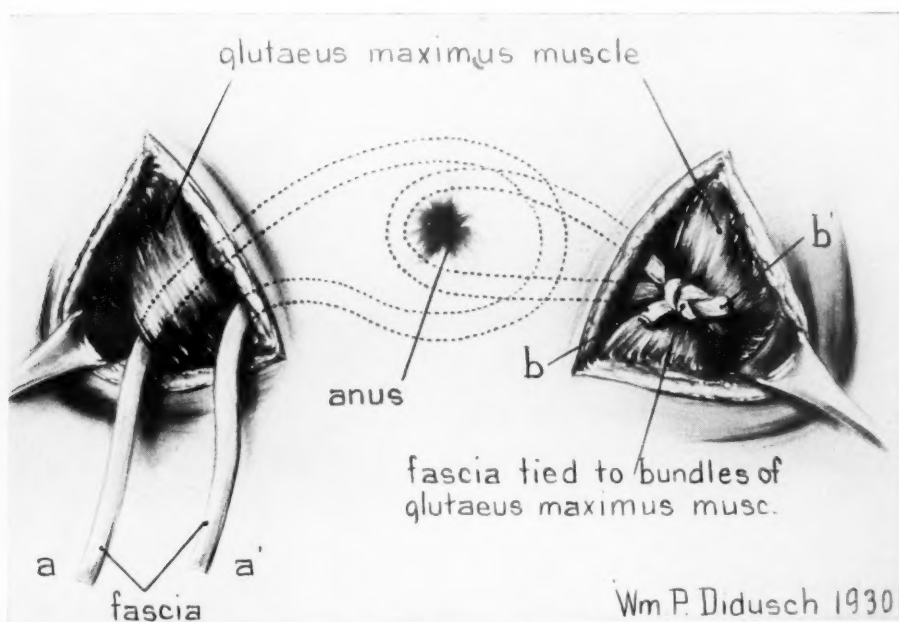


FIG. 3.—The loops of fascia are tied on the right side, ready for tying on the left. (Arch. Surg., 24, 124, 1932)

relief. A number of them were almost completely incapacitated by reason of their inability to control the anal outlet. Several had had previous unsuccessful surgical attempts directed at restoring function.

The patients ranged in age from 12 to 72 years. Twenty-one, or 70 per cent, were female; while nine, or only 30 per cent were male. There were no deaths in the group.

TABLE I

CONDITIONS WHICH DIRECTLY OR INDIRECTLY HAVE CAUSED ANAL INCONTINENCE

Condition	Number of Cases
Operation for anal fistula.....	12
Congenital abnormality.....	5
Operation for hemorrhoids.....	4
Rectal cancer (following excision of).....	2
Perineal laceration.....	2
Prolapse of rectum.....	2
Megarectum (following excision of).....	1
Trauma.....	1
Anal ulcer.....	1
Total.....	30

In Table I are presented the conditions which directly or indirectly have caused anal incontinence among this group. As would be expected this complication has occurred most frequently in connection with anal fistula. In Table II are listed the results of the fascia plastic operations. Eighty-seven per cent demonstrated some improvement, and in 40 per cent the results approximated normal control.

TABLE II

RESULTS IN 30 CASES OF FASCIA PLASTIC OPERATION FOR ANAL INCONTINENCE

Result	Number of Cases	Per Cent
Excellent.....	12	40.0
Good.....	9	30.0
Fair.....	5	16.6
Unsatisfactory.....	4	13.3
Total.....	30	

In appraising this operation, it must be remembered that certain conditions are necessary before it can have a reasonable chance of success. The gluteal muscles must be properly innervated and able to contract voluntarily. The individual must possess the intelligence to use the muscles to contract the anal canal, and the patience to practice this contraction frequently; for the measure of control given by the operation is voluntary and not automatic, as is the normal sphincter mechanism. As in all plastic operations, infection may spoil the result, and because of the proximity of the anus, infection not infrequently occurs. In six of these cases, fragments of the fascia were discharged from the wounds, but in only two of these six was the result unsatisfactory. Hence, infection and even loss of fascia may occur without necessarily jeopardizing the result. In general, the procedure has proved its value. In spite of some failures, the majority of cases have been benefited, and in certain

instances brilliant results have been obtained. It should be noted, in conclusion, that a failure does not make the patient any worse, and does not prevent a repetition of attempts by the same or other methods.

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DISCUSSION.—DR. HARRY J. WARTHEN, JR. (Richmond, Va.): I would like to add another successful case to the series Doctor Stone just reported. Several years ago I reported the case of a child six or seven years of age, born with an imperforate anus. An immediate perineal opening was made but apparently no repair to the sphincter had been attempted. In addition, the child had a megacolon. The patient was operated upon in stages, the megacolon was corrected by a lumbar sympathectomy, and Doctor Stone's fascia strips were employed to repair the anus. I saw the child for six months following operation, and each time the parents stated the control was improving. The last time they said he had complete control and no longer soiled himself. This was in spite of the fact that some infection occurred, and the child was of somewhat inferior mentality. I believe this patient was younger than any in Doctor Stone's group.

DR. DERYL HART (Durham, N. C.): I would like to report a case in which fascia was employed to replace a congenital defect in the sphincter muscle in a six- or seven-year-old girl. The sphincter muscle did not pass anterior to the rectum but ended on each side of the perineal body, where a dimple was produced by the sphincter muscle when a stimulus was applied to the perineum.

A small incision was made just posterior to the dimple on each side, and well away from the anal orifice. The sphincter muscle was located and dissected free on each side for a distance of 0.5 to 1 cm. without disturbing its point of fixation. By blunt dissection, a tunnel was made between the rectum and vagina, and connecting the two incisions. A loop of fascia was passed around the muscle on each side, pulled snug, and sutured with silk. Care was taken to avoid sufficient tension to interfere with the blood supply of the sphincter muscle. The incisions were closed, and primary healing was obtained. The child, who had had fecal incontinence since birth, had good control from the day of operation without the necessity of any educational program.

This paper was read before the Fifty-third Annual Session of the Southern Surgical Association, Hot Springs, Va., December 10, 11, 12, 1940.

ARRHENOBLASTOMA OF THE OVARY

FRED KROCK, M.D., AND S. J. WOLFERMAN, M.D.

FORT SMITH, ARK.

It is only within comparatively recent years that clinicians have begun to entertain, seriously, the thought that certain neoplasms may be able to function to a certain extent similar to the tissues from which they arise, although examples of such function have been before us for many years. For instance, Hanseemann, in 1900, observed and described the production of bile in the brain by a metastatic nodule from a primary carcinoma of the liver. In 1930, Turley somewhat clarified the situation by pointing out the similarities between neoplastic and normal cells both from the standpoint of histology and physiology. Many striking instances can be called to mind, such as hyperinsulinism due to adenomata of the islands of Langerhans, and hyperthyroidism with struma ovarii.

In 1930, Robert Meyer reported, under the term "arrhenoblastoma," a series of ovarian tumors showing, microscopically, what has been interpreted as testicular elements, and many of which possessed the bizarre property of masculinizing their hosts. As the borders of the field of endocrinology advanced, it was soon shown that this striking alteration of secondary sexual characteristics was not limited to ovarian tumors. Cushing, for instance, has reported a number of instances apparently associated with basophilic adenomata of the pituitary, and Walters found a similar picture with certain tumors arising from the cortex of the adrenal glands. As the number of reported cases increased in which the metamorphosis of the individual was associated with ovarian tumors, it became evident that even the histologic structure of the tumor was by no means uniform. In fact, a paradox appears in which the most highly differentiated tumors, namely, those in which the testicular structure is unmistakable, show the least degree of masculinization, while in the undifferentiated types, in which connective tissue elements predominate, virilism is always marked.

In 1932, we published a case report of an additional instance of an arrhenoblastoma of the ovary, classified by Meyer as belonging to the atypical group, with marked changes in the secondary sexual characteristics, and almost complete reversion to normal following extirpation of the tumor. The study of the recurrence which occurred in this particular case gives additional evidence on what may be the exact nature of some of these unusual tumors, and the report of which has been made the basis of this paper.

Case Report.—An 18-year-old schoolgirl, with amenorrhea, virilism, and hirsutism of four years' duration, was operated upon, April 14, 1932, for the removal of a large tumor of the left ovary, having the microscopic characteristics of the atypical group of arrhenoblastomata suggested by Meyer. There was a marked and prompt restoration

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to normal femininity, including resumption of a normal menstrual cycle within six weeks following operation.

One year later, the patient was apparently in good health and said that she had never felt better in her life, although a slight coarsening of the voice and increase in beard over the face was noted over what had existed at examination several months previously.

FIG. 1.

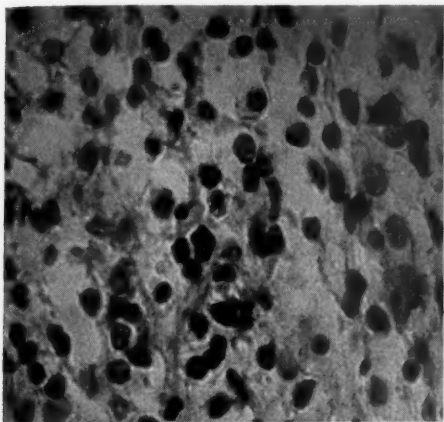


FIG. 2.

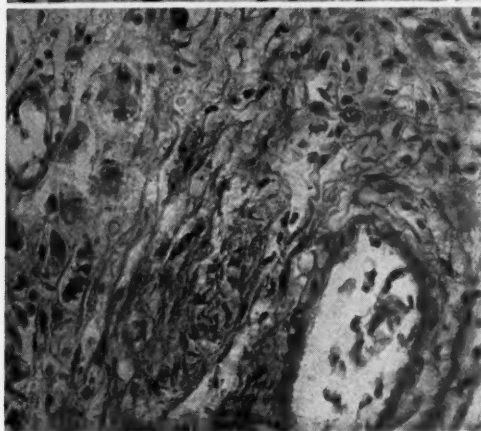
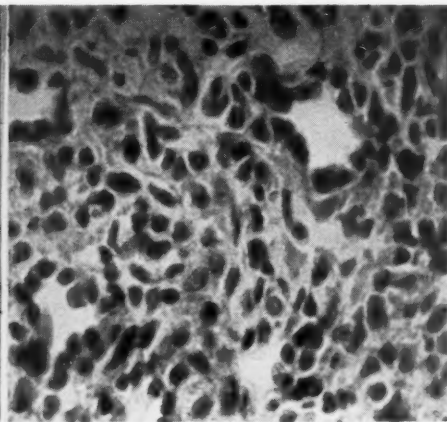


FIG. 3.

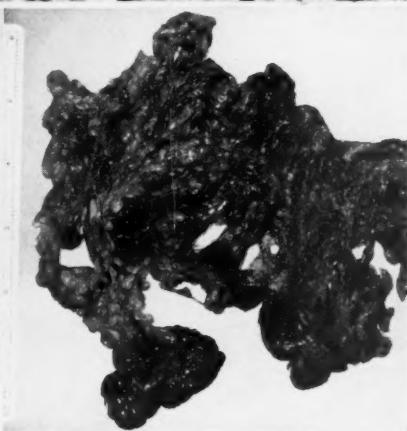


FIG. 4.

FIG. 1.—High power view of block from original tumor. Note loose, indeterminate structure.

FIG. 2.—High power field from original tumor. Note tendency to tubular formation.

FIG. 3.—Low power field from another block in original tumor. The pleomorphic character of the tumor cells is here evident and in itself suggestive of a teratoma.

FIG. 4.—Photograph of resected omentum showing the two tumor nodules of the first recurrence.

On June 1, 1933 (13 months later), while drying dishes, she turned suddenly, and was stricken with an abdominal pain of such severity that she had to be helped to a chair, where she collapsed. On admission to St. Edward's Mercy Hospital she complained of severe lower abdominal pain, and had vomited several times. On examination the patient presented an anxious facies, and appeared to be in shock. Temperature 96° F., pulse 140, weak and variable; blood pressure 90/60. There was marked tenderness in both lower quadrants but no rigidity. A blood count showed 17,000 leukocytes, with a Schilling left shift of 38. A diagnosis of acute abdominal catastrophe was evident, and exploration under ether anesthesia was carried out through the old low midline scar.

Approximately one liter of free and clotted blood was encountered upon entering the peritoneal cavity. Two tumor nodules were found attached to the omentum. The first of these was 50x30x10 Mm.; it was soft, lobulated, reddish-orange, and resembled an immature chicken egg. The second nodule measured 35x25x15 Mm., and was white, harder, and had been split in two, the fissure crossing a large omental vein which was the source of the hemorrhage. The nodules were removed with a large margin of the omentum. Further exploration showed the left ovarian region to be clear. The right ovary was 3x2.5x2.5 cm., and contained graafian follicles and corpora lutea of varying sizes and stages of development. The uterus was of normal virginal size, shape, and consistency. No other tumor nodules could be found.

On section, the first tumor was of a uniform consistency, cutting like a moderately firm lipoma. Microscopic sections of this tumor showed a loose cellular structure, with areas of rather typical embryonic cartilage (Fig. 7). A well-defined capsule surrounded the periphery.

The second nodule was harder, whitish on section, and showed several areas of hemorrhage. The microscopic structure was that of a spindle-cell sarcoma (Fig. 6) and closely resembled similar areas in the original tumor. The nuclei were large and mitotic figures testified to a rather rapidly growing process.

Convalescence was uneventful, and the patient remained in good health until August 24, 1933 (three months later) at which time she entered St. Joseph's Hospital at Booneville, Mo., complaining of abdominal pain of six days' duration and diarrhea. The following portion of the case report is from the records of Drs. Alex and C. H. Van Ravenswaay, who were kind enough to give us the follow-up:

"At this time a heavy growth of hair on face, legs and axillae was noted, with a masculine type of crines (pubic hair distribution). Chest examination, including fluoroscopy, was negative. There was a perceptible bulging in the lower quadrant, where a hard, slightly movable mass the size of a head could be easily outlined. Temperature 100° F., pulse 140; respirations 48; blood pressure 132/74. Blood examination showed 3,820,000 erythrocytes; 60 per cent hemoglobin; 17,600 leukocytes; and a differential of 90 per cent polymorphonuclear neutrophils, 6 per cent stab cells, 2 per cent myelocytes, and 2 per cent small lymphocytes. The Kahn test was negative and blood Group II. Urinalysis showed one plus albumen and three plus hyaline casts. On August 26, 1933 exploratory celiotomy disclosed a large, soft multilocular tumor, built up of mucofibrinous tissue, very friable, and adherent to the abdominal wall. It bled on the slightest manipulation. It had apparently arisen from the right ovary. Seven thousand cubic centimeters of bloody fluid were aspirated from the peritoneal cavity. Because of the danger of uncontrollable hemorrhage, and inability to completely extirpate the tumor, the abdomen was closed. Several fragments of tumor were removed for microscopic study. Blood transfusion was given postoperatively. Deep roentgenotherapy to the abdomen was started. The abdominal fluid recurred, and on September 5, 1933, 2,000 cc. were aspirated. The patient gradually grew weaker and expired, September 16, 1933. Permission for necropsy was not obtained."

The slides of tissue from this recurrence were kindly loaned to us by the Doctors Van Ravenswaay for study. Part of the section consists of closely packed round nuclei with practically no intercellular substance, and resembling, grossly, a smear from tissue rather than cut sections (Fig. 8). The nuclei, for the most part, are round and hyperchromatic, and variable as to size. The majority are macrocytic. In a few areas, the nuclei are arranged in the form of rudimentary tubules (Fig. 9), resembling the structure seen in the original tumor. Differentiation, on the whole, is very poor. The tissue is abundantly supplied with poorly constructed capillaries distended with erythrocytes. No whorls or spindle cells are noted in these areas.

Adjacent areas show a mucoid type of connective tissue, reminiscent of Wharton's jelly in the umbilical cord. Definite wavy fibrils are interspersed between the spare nuclei. Both spindle-shaped and large, round nuclei are evident, with the latter pre-

dominating. Mitotic figures and atypical cell divisions are abundant. The cells themselves are circular with interlacing fibrils.

Probably no chapter in oncology offers more exciting possibilities for speculation than does this interesting group of masculinizing ovarian tumors. In the first place no present-day classification of ovarian tumors is entirely satisfactory from the standpoint of morphogenesis. Explanation of the origin of comparatively simple forms, such as pseudomucinous cystadenomata and papillary types, leaves much to be desired. It is little wonder, then, that in dealing with complex neoplasms, such as the various forms of the so-called arrhenoblastomata, we fully unleash our imaginations in the attempt to correlate physiologic manifestations with morphology as a key to the solution. A number of theories have been advanced, the most prominent of which are:

(1) *Hermaphroditic Basis*.—Pick first suggested that these tumors might be associated with hermaphroditism or pseudohermaphroditism. As the number of reported cases increased, it soon became apparent that this view was not tenable, because, as a rule, the individual has developed anatomically and physiologically along perfectly normal female lines until the tumor began to manifest its presence by a transformation of secondary sexual characteristics. In other words bisexuality was not present from birth, as must obtain with true hermaphroditism.

(2) *Gonadal Protective Effect*.—Halban has insisted that the zygote is primarily male, female, or hermaphroditic from the moment of fertilization, and that the gonads exert only a protective effect and not a formative influence upon the development of secondary sexual characteristics. In other words, all the primary and secondary sexual characteristics of the individual are established from the beginning. For the full development of the secondary sexual characteristics, a protective effect from the gonads themselves is necessary. The tendency of certain tumors to change the secondary sexual characteristics can then be explained by assuming that the tumor is able to exert an hyperprotective effect upon latent male elements present. When the tumor is extirpated, reversion occurs because of the withdrawal of the male protective influence, and further suppression by resumption of normal ovarian function.

(3) *Origin of the Tumor from Latent Male Elements*.—Robert Meyer, under the term "arrhenoblastoma," groups together a rather heterogeneous collection of ovarian tumors varying from apparently typical testicular adenomata, without endocrine effects, to spindle-cell sarcomata, with an occasional rudimentary tubule and associated with extreme masculinization. He suggests the explanation that the cell mass destined to become the sex gland is at first indistinguishable as male or female, and that, eventually, cords of cells appear beneath the germinal epithelium, and extend down toward what later becomes the hilum. In the male, these structures become permanent as seminiferous tubules, while in the female, atrophy takes place and they remain as abortive seminiferous tubules or medullary cords. The true ovarian struc-

ture is then built up around them and, as Novak expresses it, "they become fossilized in the rete ovarii." Meyer feels that these cell remnants retain their male potentialities, and may give rise to tumors with masculinizing tendencies. The stumbling block here is that no one has an adequate ex-



FIG. 5.—Drawing of tumor nodule of first recurrence, with tear into omental vein and subsequent hemorrhage.

planation of just what factor enters into the picture to cause these presumably normal cells to spring into such vigorous activity as to overcome all previously fully developed ovarian tissue.

(4) *Teratomatous Origin.*—Popoff, in 1930, in reporting a case of testicular adenoma of the ovary suggests that these tumors may represent one-sided teratomata, citing Ewing's similar conclusion as to the origin of embryonal carcinomata of the testicle, and L'Esperance's concerning embryonal carcinomata of the ovary. Büttner, in a report of 25 cases collected in 1932, raises the question whether an arrhenoblastoma may not be, after all, only a teratoma of the ovary in which the other tissue elements, usually found in teratomata, are lacking due to their destruction by sarcomatous degeneration. Pick has definitely stated that a single element in a teratoma may predominate and obscure, or even suppress, all other tissue elements. Attention was called by us, in 1933, to the possible teratomatous origin of these tumors, after finding of cartilage in the first recurrence in our case. McLester and Ledbetter, in 1936, reported further definite confirmatory evidence of this view, in their case.

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TABLE I
TABULATION OF REPORTED CASES
Modified from Baldwin-Gafford

Author	Age	Involved Side	Pathologic Anatomy
1. Pick	34	Right	Typical testicular adenoma, right ovary
2. Schickele	26	Left	Typical tubular adenoma
3. Neumann	32	Typical tubular adenoma. Interstitial cells
4. Berner	22	Typical tubular adenoma
5. Blair Bell	19	Right	Part tubular; part solid. Interstitial cells
6. Meyer	46	Left	Carcinomatous tubular adenoma
7. Meyer	47	Right	Carcinomatous tubular adenoma
8. Neumann	56	Both	Carcinomatous tubular adenoma
9. Meyer (Priebatsch)	44	Carcinomatous tubular adenoma
10. Meyer (Phelan)	20	Left	Typical testicular adenoma
11. Miller	30	Left	Typical testicular adenoma. No masculinizing
12. Popoff	31	Right	Tubular adenoma with solid portions
13. Meyer (Cupei)	16	Left	Part typical; part atypical; and part solid carcinomatous
14. Meyer (Univ. Clin.)	23	Right	Major portion atypical
15. Meyer (Bauer)	66	Left	Part tubules
16. Meyer (Mackenrodt)	35	Right	Cords and portions similar to granulosa cells
17. Meyer	31	Solid epithelial cords. Narrow openings
18. Meyer	36	Tubules. Dense epithelial infiltration
19. Spielman	26	Right	Tubules and cords
20. Novak-Long	20	Left	Definite tubules. Also typical sarcoma
21. Szathmary	25	Right	Marked polymorphism. Large solid areas and areas of epithelial tubules
22. Moots	..	Left	Tubules. Fibroblastic sarcoma
23. Meyer (Orru)	40	Left	Pseudomucinous tumor
24. Meyer (Knebel)	28	Left	Mucous membrane in tumor
25. Meyer (Specht)	26	Left	Granulosa cells in tumor
26. Halban	31	Small-celled carcinoma; solid with tubular shapes
27. Wagner	25	Left	Epithelial solid tumor. Tubules
28. Kleinhans	31	Left	Rests of epithelial new growths. Regressive changes
29. Krause	41	Recurrence R.	Epithelial cord-like arrangement
30. Geisler	..	Right	Cord-like carcinomatous tumor. Mucous epithelial rests
31. Strassmann	24	Right	Atypical adenoma; part carcinoma; part sarcoma; mucous cysts
32. Sedlis	16	Left	Epithelial strings; partial tubular; cystic degeneration
33. Taylor-Wolferman-Krock	18	Left	Irregular medullary cords. Rudimentary tubules. Cartilage in recurrence
34. Eerland	35	Right	Solid periphery with cystic areas within; tubules and cords
35. Baldwin-Gafford	24	Left	Most of tissue sarcoma; primitive tubules and cords. Bone formation
36. Sellheim	47	Solid epithelial tumor
37. Bingle-Schultze	47	Strings and fields of epithelial cells
38. Mathias-Tschirdewann (Sedlaczak)	19	Solid tumor. Tissue resembling thyroid
39. Buettner	66	Left	Solid epithelial tumor. Strand-like villous and tubular portions
40. McLester	32	Right	Cyst containing mucous producing cells; fat; cyst with ciliated columnar epithelium; gland-like epithelial cells
41. Benecke	28	Left	Tubules; mucous cysts; sarcomatous portion
42. Benecke	26	Left	Cavernous network of cells
43. Norris	34	Right	Cords of epithelial cells
44. Hitzanides	19	Right	Sarcoma. Cubical carcinomatous cells
45. Foderl	17	Left	Tumor suggesting fibroma. Proved to be epithelial
46. Depuy	61	Atypical arrhenoblastoma
47. Anderson	..	Right	Alveoli; tubules hypernephroma-like cells. Interstitial cells
48. Haffner	32	Right	Cystic. Pseudomucinous substance. Interstitial cells. 18 mouse units of folliculin in 24 hr. urine

Author	Age	Involved Side	Pathologic Anatomy
49. Glaser-Erhard-Haempel	27	Left	Spindle cells. Mucous elements (fibroma with mucoid degeneration). Calcium deposits
50. Kleistman	30	Left	Large cells with nuclei. Protoplasm contains drops of fat
51. Pires	22	Left	Papilliferous cystadenoma with sarcomatous degeneration. Tubules; cords. Lutein-like cells. Supra-renal cortex
52. Xavier-Junqueira	34	Right	Tubules; cords. Granulosa cells. Histologic picture pleomorphic
53. Kleine, H. O.	54	Right	Tubules; spindle-form cells. Interstitial cells
54. Kleine, H. O. (P. Wolff)	49	Right	Tubules. Interstitial cells
55. Kleine, H. O.	55	Both	(Teratoma in left ovary) skin, hair, fat, bones. Right showed tubules, interstitial cells, sarcoma
56. Kleine, H. O. (Bachel)	52	Right	Tubules; solid cords; interstitial cells
57. Schiller	17	Left	Interstitial cells; epithelial cords
58. Dockerty-MacCarty	25	Left	Alveolar cells; interstitial cells
59. Dockerty-MacCarty	31	Left	Testicular tubular adenoma. Absence of interstitial cells. Marked virilism
60. Dockerty-MacCarty	15	Right	Cords; tubules; interstitial cells
61. Dockerty-MacCarty	51	Right	Tubules; cords; no interstitial cells. No clinical virilism. Recrudescence of bleeding
62. Neumann	..	Left	Tubular testicular adenoma
63. Cabot case: No. 25351	29	Right	Well-formed tubules. Adenoma tubulare testiculare. Interstitial cells.
64. Boltuch	28	Left	Connective tissue tumor. Cysts with cuboidal epithelial lining. Interstitial cells. No tubules. Epithelioid cells
65. Luzuy	16	Right	Fibromyoma; cuboidal epithelial cells. No tubules. Interstitial cells
66. Aburel-Marza-Dobrovici	22	No true tumor. Two nodules; glandular tubules. Interstitial cells. No virilism
67. Sarkar-Tribedi	18	Left	Tubules; sarcoma. Different sections showed different types of cellular pattern
68. Wijnenbeek-Plate	28	Left	Multicameral cyst. Tubules. Fat-containing cells resembling interstitial cells
69. Hardjosoekatmo	23	Left	Mucous cysts. Epithelioid cells. Tubules
		Right recurrence Death from recurrence	
70. Xavier-Junqueira	43	Right	Sarcomatous degeneration. Epithelial cysts. Deep yellow pigment. Tubules. Interstitial-like cells

With this theory in mind, we have studied all the available reports on cases listed as arrhenoblastomata in the literature, and have been able to collect 70 cases (Table I). A study of this material would seem to point toward several significant facts: In the first place, the conclusions of investigators on sex reversal, that the right ovary exhibits testicular transformation more often than the left in animals, is not borne out in the human, since the tumor was found on the left side in 31 cases as against 26 cases on the right. The affected side is not mentioned in 11 cases, and in two it was stated as occurring on both sides. It is also to be noted that the histologic pictures, as reported, lack the necessary degree of uniformity to be convincing that this unusual tumor is a distinct pathologic entity. And, lastly, we have been able to find 24 instances in this group of cases in which suggestions of tri-dermal tissue elements were found on routine examination (Table II).

Since Ewing has reported finding only a single island of cartilage and a single epidermoid nest in a large embryoneal carcinoma of the testis, or teratoma in serial section, it would seem only reasonable that this method of

ARRHENOBLASTOMA OF OVARY

study applied to these tumors would yield an even greater percentage of tri-dermal tissue elements than was found in routine sections. In our own case, a section from each of 50 blocks from different portions of the tumor was studied, but this is still an infinitesimally small number in a tumor weighing 990 Gm.

FIG. 6.

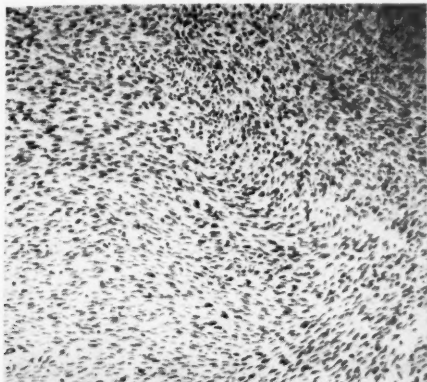


FIG. 7.

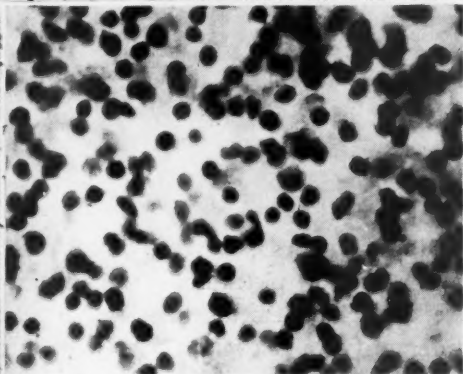
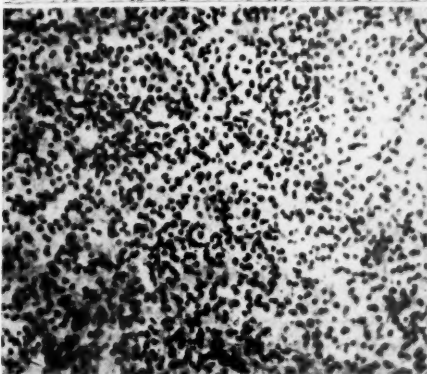
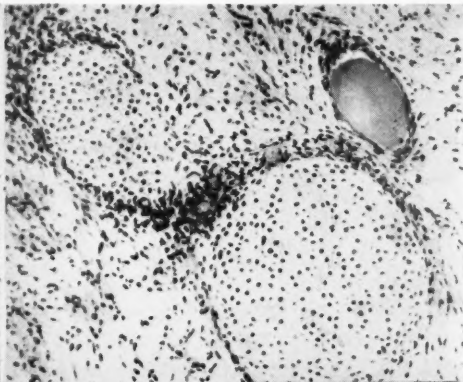


FIG. 8.

FIG. 9.

FIG. 6.—Low power field from one of the nodules removed during the first recurrence. The same spindle cell sarcomatous structure appears here as was found in the original tumor.

FIG. 7.—High power field from the second nodule removed during the first recurrence. Typical cartilaginous islands are apparent.

FIG. 8.—Low power field from second recurrence. Note anaplastic type of growth.

FIG. 9.—High power field from second recurrence. Note tubule formation, and similarity of structure of original tumor as shown in Figure 2.

In a number of the reported cases, the presence of interstitial cells is noted, the identification of these cells being based upon morphology as well as their affinity for fat stains such as Sudan III. Popoff in his case of testicular tubular adenoma of the ovary showed, definitely, that these large clear, fat laden cells were epithelial cells which had undergone lipoid degeneration, rather than being true interstitial cells which are considered to arise from mesodermic elements.

Alteration of secondary characteristics in the female is not limited to one particular group of ovarian tumors. We find, in the literature, many reports of masculinizing ovarian tumors in which histologic examination has failed to

disclose the presence of testicular elements, even by men familiar with Meyer's work. Studdiford, for instance, reports a case of granulosa cell carcinoma which produced clinical masculinization, and cites Bergstrand, of Sweden, as

TABLE II
TRIDERMAL TISSUE ELEMENTS FOUND IN 70 CASES

Tissue Elements	No. of Cases
Mucous membrane.....	9
Granulosa cells.....	3
Cartilage.....	1
Bone.....	1
Thyroid.....	1
Ciliated epithelium.....	1
Pseudomucinous tissue.....	2
Lutein cells.....	1
True teratoma.....	1
Sarcoma.....	2
Suprarenal cortex.....	1
Fat.....	1
Total.....	24 or 34%

having seen several similar cases, and who subsequently studied some of Meyer's material and reclassified it as granulosa cell carcinoma. Maxwell's case proved to be aberrant cortical tissue in the ovary. A case reported in the Massachusetts General Hospital clinicopathologic conferences with a typical picture of acquired virilism, with regression to normal after operation, was found by Mallory to be an embryonal carcinoma of the ovary. Lutein cell tumors, dermoids and true teratomata, with clinical virilism, have been reported by Schiller, Cosascesco and others. Goldberg records a case of true sarcoma of the ovary with masculinization.

In other words, we have, on the one hand, the so-called "arrhenoblastoma" with a variable picture of masculinization clinically but with what apparently are testicular elements histologically, and, on the other hand, a number of different types of ovarian neoplasms in which the predominant tissue is other than testicular, but with clinical virilism. The one thing common to two such widely divergent pictures is the presence of tridermal tissue elements, which can be demonstrated by routine studies in approximately one-third of the cases. To create a new pathologic entity, based upon the predominant tissue present, as has been done with arrhenoblastomata, would lead to hopeless confusion. In the final analysis, our present knowledge is still deficient concerning the exact origin of all the factors controlling the development of secondary sexual characteristics. Upon this basis, it is our plea that all masculinizing ovarian tumors be classified as teratomata with a one-sided development, be such development testicular elements (either in the form of interstitial cells or seminiferous tubules), adrenal cortical remnants, or even other tissues or their anlagen whose rôles at present under normal conditions, in the development of the secondary sexual characteristics of the individual, are not fully understood. Or we may retain the term "arrhenoblastoma" to indicate such a "clinicopathologic" condition as suggested by Norris, rather than regard it as representing one constant pathologic entity to be pigeon-holed thus by any pathologist inspecting the tissue microscopically.

CONCLUSIONS

(1) The final follow-up on a previously reported case of arrhenoblastoma of the ovary is presented.

(2) Evidence is brought forth to support the conclusion that, from a purely pathologic standpoint, arrhenoblastomata may represent one-sided teratomata.

The authors wish to express their appreciation to Dr. J. L. Goforth for the excellent photomicrographs presented, and to the Doctors Van Ravenswaay for allowing us to report the final follow-up from their case records, and for the loan of slides showing the terminal stages of the tumor.

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DISCUSSION.—DR. EMIL NOVAK (Baltimore, Md.): The first case of arrhenoblastoma reported in this country under that designation was the one whose later history has just been described by Doctor Krock. Similar tumors had been previously described, but under incorrect diagnoses, as the pathologic entity now designated as arrhenoblastoma was then not known. We now have in our laboratory specimens or slides of 11 of these rare tumors, though most of these have been sent in for diagnosis from outside sources.

Doctor Krock has laid especial stress upon the finding of teratomatous elements in a number of the reported cases, and suggests, as others have done, that arrhenoblastoma is to be looked upon as of teratomatous origin. I do not think that the evidence can be considered convincing. Dysgerminoma, in my experience, is more apt to be associated with teratomatous elements than is arrhenoblastoma, but this does not justify the conclusion that it is in itself a type of teratoma.

No one, of course, can speak with assurance as to the etiology of arrhenoblastoma and I, for one, do not feel convinced of the entire adequacy of the generally accepted theory of Robert Meyer, who has done so much to clarify this subject for us. We know too little, as yet, of the factors concerned in sex differentiation. It has always seemed significant to me that the anlage of the adrenal cortex in the early embryonic phase is directly continuous with, and indistinguishable from, that of the ovarian medulla. This may explain why certain tumors of the adrenal cortex and such ovarian medullary tumors as arrhenoblastoma produce identical clinical pictures, especially as regards masculinization phenomena.

There is no stereotyped histologic picture in arrhenoblastoma, and the term really refers to an histologic family rather than to any one histologic type. To interpret and diagnose these tumors one must have some idea of the early embryology of the ovary.

From a clinical standpoint, the early symptoms of arrhenoblastoma, such as amenorrhea and flattening of the breasts, are not to be looked upon as masculinizing, but rather as merely defeminizing, that is, subtracting something from the feminine characteristics of the patient. Later come the more positive evidences of masculinization, such as hirsutism, deepening of the voice, and hypertrophy of the clitoris. Hirsutism, in itself, is certainly not always a sign of masculinization, for it is often found in women who otherwise are typically feminine, and who menstruate normally and bear numerous children. It may, however, form a part of the masculinization syndrome, when combined with other such symptoms as I have mentioned.

I make this distinction because the mistake is often made of suspecting arrhenoblastoma when an ovarian tumor is found in a woman who also exhibits the picture of the so-called virilism. The latter, however, will usually be found to have been present since puberty, and it will not disappear after removal of the tumor, which will be found not to be an arrhenoblastoma. When, on the other hand, a previously normal woman develops masculinization phenomena, and an ovarian tumor can be palpated, the suspicion of arrhenoblastoma is fully justified, though, even then, mistakes will occur. An exactly similar picture can be produced by certain rare adrenal tumors of the ovary, while in some cases a tumor of the adrenal cortex, combined coincidentally with a simple cystadenoma of the ovary, may simulate, perfectly, the characteristic syndrome of arrhenoblastoma.

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CARCINOMA OF THE FUNDUS OF THE UTERUS

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THERE ARE varied opinions concerning the best treatment for the patient with carcinoma of the body of the uterus. Masson and Gregg¹¹ feel that the standard treatment of carcinoma of the body of the uterus is a total hysterectomy with bilateral salpingo-oophorectomy. Richardson¹⁵ stated, in 1935, that the complete surgical extirpation of the uterus together with both tubes and ovaries still remained the best therapeutic attack on cancer of the corpus uteri. Sackett,¹⁶ in 1937, preferred combined therapy whenever it was possible. In 1937, Scheffey and Thudium¹⁹ advocated preliminary irradiation with a panhysterectomy in selected cases. Martin¹⁰ takes the position, that if a curettage after irradiation showed malignant tissue, then an operation was advised for certain groups. Kilgore⁸ stated that, in 1936, the California Cancer Commission recommended an hysterectomy with preoperative irradiation in cancer limited to the uterus, and irradiation therapy in cancer extending beyond the walls of the uterus. Because of these varied opinions, the writer has made a study of a group of our own cases, with particular endeavor to evaluate the end-results of treatment.

There were 110 case records of patients with this pathologic entity, who had been seen in the Scott and White Clinic during the 20-year period, from 1921 through 1940. Eighteen patients of this number were excluded from this study. Six of the 18 had been treated elsewhere, and came to the clinic for observation only. Four others declined treatment, and eight were found to have diffuse metastasis and were regarded as hopeless, so no treatment was advised. The remaining 92 patients, of the 110, entered the hospital for treatment, and they form the basis for this detailed review. The diagnosis of carcinoma of the uterine fundus was proved histologically in every case. Follow-up data to date have been obtained on all patients. All patients with both cancer of the uterus and of the ovary were omitted from this study except two. In these, there was little question but that the cancer was primarily of the uterus. Cancers of the fundus and cervix were excluded also, unless the lesion was rather definitely primary in the corpus.

The incidence of carcinoma of the fundus is decidedly less than is that of the cervix. Sackett¹⁷ reported the ratio of body carcinoma to that of the cervix, as one to five; Crile and Elias,⁴ one to three; Scheffey and Thudium,¹⁹ one to nine and five-tenths. The incidence in our clinic has been approximately one to six. During this same period of time, 17 patients have been seen with sarcoma of the uterus. In our clinic, there have been seen six

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cancers of the cervix to one of the fundus, and six carcinomata of the fundus to one sarcoma.

The etiology of fundal cancer remains obscure. Taylor,²¹ after an extensive study of the problem, wrote that the relationship of hyperplasia to carcinoma of the endometrium has an etiologic and clinical aspect. He reported

TABLE I
THE AGE INCIDENCE

Age	No. of patients	Age	No. of patients
30 to 40 . . .	3	60 to 70 . . .	19
40 to 50 . . .	16	70 to 80	5
50 to 60 . .	49		

The average age was 55.
19 or 20.6 % were under 50.
73 or 79.4 % were over 50.

the association of endometrial hyperplasia and carcinoma in the same uterus. McMurrey⁹ concludes that a functional abnormality is present in the reproductive organs of women with this condition. Counsellor³ suggested that this type of cancer is in one manner related to the ovarian hormones. Herrell⁷ wrote: "It seems reasonable to conclude that the unopposed action of estrin with its resulting effect on the endometrium is the basic principle at work in the development of malignancy of the endometrium of those individuals who possess the genetic factor necessary for the development of cancer."

It is the consensus of opinion that parity is not an etiologic factor. In this case review, it was found that 87 were married and five were single. Seventy-three per cent of the married women were mothers. Fibroid tumors are considered to have but little if any etiologic significance in this disease; however, the development of cancer from endometrial polyps does occur. Thirteen patients of this series were found to have uterine polyps.

Crossen and Hobbs⁵ found that cancer of the uterine fundus tended to occur, definitely, more often in the woman who had a late menopause. Therefore, the patient with a history of a late menopause should cause us to suspect some type of endometrial lesion. In our study, it was found that 65 patients, or 70.6 per cent, developed symptoms after the menopause and 27, before the menopause. The average time of the menopause, in those patients who had cancer beginning after the climacteric, was 49 years.

Patients with cancer of the uterine body are definitely older on the average than are those who have a malignancy of the cervix. A majority of statistics shows that the average age incidence is in the late fifties. Healy and Brown⁶ gave the average age incidence as 55. Counsellor wrote that 90 per cent of these patients were over 45. Our statistics showed that 19 patients were under 50, and 73 were over 50 years of age. The average age was 55 years, 79.3 per cent being past 50 (Table I).

The cardinal signs and symptoms are a metrorrhagia, a menorrhagia, a vaginal discharge, and pain. We would stress the significance of abnormal vaginal bleeding, which is the predominant sign of this condition. According to Norris and Dunne,¹³ it is the first sign in 80.5 per cent of the cases. Pratt¹⁴

found, in a study of 71 cases, that there was microscopic to gross bleeding in all of the 71 cases. We found that 24 of the 27 patients, who developed cancer before the menopause, gave histories of prolonged or irregular bleeding. Sixty-two of the 65 patients, who had symptoms after the menopause, gave bleeding, or a blood-tinged discharge as their most significant symptom. Abnormal vaginal bleeding was the symptom of first importance manifested by 93.5 per cent of the entire group. The fact should be emphasized that the postmenopausal bleeding is usually small in amount, and sometimes it is just a spotting. It may occur at intervals of a few or several weeks, or even several months. Profuse bleeding, which happens with so many benign conditions of the uterus, is seldom seen in carcinoma of the fundus, except occasionally in advanced cases. Because of the small amount of bleeding at infrequent intervals, seen in many cases, it is difficult for the patient to appreciate its significance. Patients quite frequently regard the change in amount and character of flow as a natural accompaniment of the menopause and, therefore, defer consulting a physician. It is hard to evaluate the significance of a vaginal discharge for there are so many pathologic conditions which produce discharges. However, a number of patients with uterine malignancies do give histories of a brownish, watery discharge, sometimes irritating in nature.

Pain is a symptom in approximately one-third of the patients with carcinoma of the fundus of the uterus. Healy and Brown reported its occurrence in 32 per cent of the patients. Thirty-one, or 33.7 per cent, of the 92 patients of this group studied, made a complaint of some degree of pain. It was usually in the nature of an aching, a discomfort, a heaviness, or sometimes a cramping menstrual type of pain. The pain was seldom of an intense degree. It should be remembered that early cancer anywhere does not cause actual pain. It can be readily appreciated, however, that late cancer, with metastasis, does produce definite pain and, as stressed by Healy and Brown, when the patient complains of rather persistent actual pain, metastasis or extension of the carcinoma, frequently, has occurred. Our study would tend to substantiate their observation that a definitely smaller percentage of patients are cured who complain of pain.

It is practically impossible to accurately ascertain the duration of symptoms in some cases. In some instances the first symptoms of disease were due probably to benign lesions, which later underwent malignant change. We calculated the average duration of symptoms in this group to be ten months before the patient came to treatment.

A careful physical examination is important as an aid in arriving at a correct diagnosis and often, also, in deciding the preferable plan of treatment. The size, the shape, the irregularities, and the mobility of the uterus, particularly, should be observed. It should be determined if there is either a thickening or masses in the broad ligament regions or in the culdesac, for masses may be due either to metastasis from the uterine cancer or to a benign tubo-ovarian pathologic condition. The cervix should be carefully examined, for malignant tissue or a polyp may be observed protruding from the external os. Blood

may be seen coming from the cervical canal, establishing definitely the source of the bleeding, and occasionally a metastatic malignancy will be seen on the vaginal mucosa. The incomplete physical findings, noted in some of our own records, emphasize the importance of an accurate physical examination. The physical findings, however, are essentially negative, for in about one-third of the patients with this pathologic entity, and in this group reviewed, the size of the uterus of 31 patients was considered normal. The uterus was moderately enlarged and less than the depth of six inches for 51 patients; while it was found to be markedly enlarged for ten patients.

There is only one accurate diagnostic procedure. It is a carefully performed curettement, with examination of the curettings by a competent pathologist. Sometimes, upon gently dilating the cervix, malignant tissue will begin to discharge from the uterine canal. Frequently, this will be sufficient tissue from which to make an histologic diagnosis. However, usually, a methodical curettement, with careful examination of all curettings should be done. Cautious sounding of the uterus should be made to ascertain its shape and depth. All manipulation within the uterus should be of a gentle nature in an attempt to prevent the dissemination of carcinoma cells through the lymph or venous channels or through the tubes. Irregularity of the contour is sometimes due to fibroid tumors, for these are reported present in 25 per cent, or more, of such cases. Stacy²⁰ reported fibroid tumors present in 37.23 per cent of these cases. Twenty-three of our 92 patients, or 25 per cent of this group, had fibroid tumors. Morrin and Max¹² found that 35.2 per cent had fibromyomata, but only 5.6 per cent of the fibromyomata had associated cancer. While the association of fibroid tumors is not regarded as a material etiologic factor, they do, sometimes, mask the symptoms of the cancer. To conclude that all postmenopausal bleeding is due to cancer, is erroneous. Wittenbourg and Zlatmann²² collected from the literature 2,384 reports of postmenopausal bleeding. They found that the incidence of malignancy was 62.8 per cent. Unquestionably, radical surgery should not be performed with only a history of abnormal uterine bleeding. It is essential that a positive diagnosis be made first. However, caution must be exercised to the end that the bleeding due to cancer not be attributed to benign tumors. We would emphasize the importance of a thorough study of all curettings of patients with uterine fibromyomata, and furthermore, the necessity of an immediate opening and examination by the pathologist of all uteri removed for supposed benign disease. Nine patients of this group were operated upon with a pre-operative diagnosis of benign conditions, and when the uteri were opened after removal, there were found carcinomata within the fundi.

The anatomy of the uterus and the pathology of fundal cancer modify treatment. The cancers of the body of the uterus are usually adenocarcinoma. The disease is one primarily of the endometrium; therefore, at the beginning it is encased in the thick, muscle-walled cavity. There are no racemose glands extending from the endometrium into the myometrium, as are found in the cervix. The lymph supply to the fundus is sparing in nature, and the

lymphatic dissemination is late, for it is unlikely to occur until after the muscle wall has been deeply penetrated by the malignant process. Usually, the spread of the disease into and through the muscle wall is slow, requiring many months, and in some instances, years. An early case of our group emphasizes this fact. This patient had a papillary adenocarcinoma, Grade II, of the fundus, which was treated by intra-uterine application of radium. Nine years later she returned with the history of a spotting and pinkish discharge

TABLE II
DEGREE OF ACTIVITY OF
CELL MALIGNANCY

Grade	Number of patients
I	12
II	46
III	28
IV	2
Not Graded	4

65.9% were of low-grade malignancy.

TABLE III
GRADE OF MALIGNANCY IN RELATION TO AGE
AND MENOPAUSE

Grade	Average age	Pre-menopause	Post-menopause
I	48	6	6
II	53	13	32
III	58	3	24
IV	59	0	3

The low-grade malignancies tend to occur in the younger group.

for a duration of four months. On repeating the curettage, the scrapings showed the same pathologic finding as they did nine years previously. Radium was again applied followed by roentgenotherapy. This patient is now apparently well, and it is two years since the last treatment. Such observations tend to support the view that a cancer of the uterine fundus often remains a local disease for many months or even a few years. It is a fortunate fact, favorably influencing treatment, that a majority of these lesions are of low grade in degree of cell activity. In this series, 58 cases, or 65.9 per cent, were found to be either Grade I or Grade II; or, approximately, two out of three of these patients had a malignancy of low degree (Tables II, III and IV).

Three methods of management used in treating body cancer are irradiation therapy; surgical extirpation; and a combination of the two. Three factors are to be carefully considered in planning treatment for an individual case: The degree of malignancy; the extent of the disease; and the physical build and the status of the general health of the individual. These three factors, together with the plan of management instituted, largely determine the percentage of cures. The extent of the disease is the most important factor modifying the results of treatment. This is true because most lesions are curable when treated early, notwithstanding the degree of cell activity or the physical status of the patient.

Practically all patients in this series have been treated by one of two methods—irradiation therapy; or the combined method of irradiation and surgery. The procedure followed, usually, was an exploratory curettage for all patients with a suspicious history with an immediate frozen-section of the curettings by the pathologist. If the microscopic examination showed the presence of a malignancy, radium was applied at the time. If the lesion was believed an operable one, and if the physical status of the patient was favorable

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for surgery, usually a panhysterectomy was performed some six to eight weeks following the radium treatment. In the group of patients treated by irradiation alone, roentgenotherapy was begun two to eight weeks following the radium application, and from one to three series at two months' intervals usually were administered. For the group accepting surgery, the first roentgen

TABLE IV
CURABILITY ACCORDING TO GRADES

5-Year survival			
Grade	Survived five years	Dead	Percent of cures
I	7	1	87.5%
II	20	15	57.4%
III	10	9	52.6%
IV	1	0	100%

The degree of malignancy definitely modifies curability.

series was begun from three to eight weeks after the operation. Roentgenotherapy was used particularly to fortify against regional metastasis.

A review of these 92 cases showed that 31 patients were treated more than five years ago exclusively by irradiation therapy. Thirteen patients, or 41.9 per cent, lived from five to 13 years; however, one of these is known to have died later of cancer (Table V). Eighteen patients, or 58.1 per cent, died before the end of five years; however, two of these deaths were due to intercurrent disease. Thirteen patients have been treated within the last five years by irradiation therapy. Eight of these patients are alive to-day. Of the five dead, one lived for four years and died from diabetes. Another died within one year of an acute respiratory infection. The patients who were treated by radium and lived five years or more were given an average of 3,500 mg. hours. The patients who were given radium and lived less than five years were given an average of 3,800 mg. hours.

There were 24 patients who were treated more than five years ago by preliminary irradiation and then surgery followed by roentgenotherapy. Nineteen or 79.1 per cent, of these patients were apparently well from five to seventeen years after treatment (Table VI). Five of the 24 patients are dead, but one of the five is known to have died of an intercurrent disease. Ten patients have been treated during the last five years by this procedure, and all but one are living at this time, and apparently free of disease. It is noteworthy that the highest percentage of cures has been obtained by this method of management. The statistics of these two groups would seem to support our conviction that intrauterine irradiation therapy, followed by a panhysterectomy is the preferable treatment for the patient with a carcinoma of the fundus, when the disease is still limited to the uterus, and the patient is a reasonable surgical risk. However, it is realized that a comparison of the statistics of these two methods of treatment does not give a correct evaluation

of the relative merits of the two plans of management, for a definitely higher percentage of the more favorable cases were treated by the combined procedure.

Sixty-six patients with cancer of the fundus of the uterus have been treated by various methods, treatment having been completed more than five years ago, and a study of the end-results shows that 40 patients, or 60.6 per cent,



FIG. 1.—Residual adenocarcinoma in fundus following 3,600 mg. hrs. radium eight weeks previous.

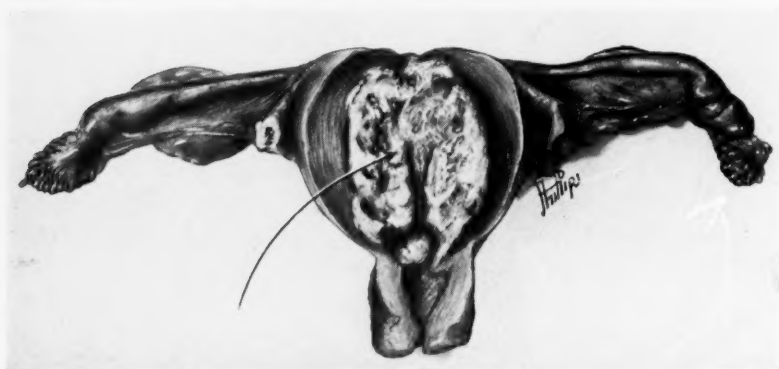


FIG. 2.—Large residual adenocarcinoma in fundus following 2,400 mg. hrs. radium six weeks previous.

lived from five to 17 years after receiving treatment. Hysterectomies have been performed for 48 patients. There was only one death, or a mortality rate of 2.1 per cent. There were no deaths from radium therapy; therefore, the mortality rate of the 92 patients treated is only one death, or 1.1 per cent.

Discussion.—Thirty-four patients were given radium and later the uteri removed. A pathologic study of these uteri showed that carcinoma was still present in 18, or 55.8 per cent. No cancer cells were found in 16 specimens, or in 44.2 per cent of the removed uteri. Healy and Brown reported that cancer cells were found present in 60 per cent, or 41 of 69 uteri removed after

irradiation therapy. However, they also found that when a large dose of radium was given, cancer cells were present in only 40 per cent of the removed uteri. Corscaden² reported residual cancer in 61.9 per cent of the post-irradiated uteri. Sackett stated that at least one out of three hysterectomy specimens showed persistent cancer after irradiation (Figs. 1 and 2). The smallest dose of radium administered to any of our patients, upon whom an hysterectomy was later performed, was 800 mg. hours, and the largest dose was 4,800 mg. hours. The average radium dosage was 2,600 mg. hours for those uteri in which no cancer was found present, and 2,500 mg. hours for those uteri in which cancer was found present. Fifteen patients have been observed more than five years who had cancer present in the removed uteri, after previous irradiation. Eleven of these patients, or 73.3 per cent, were well after five years. Nine patients have been observed more than five years who had no cancer cells present in the removed uteri, following preliminary irradiation. Eight of these nine patients, or 88.8 per cent, have remained well.

During the first years of the time included in this review, the dosage of radium was not standardized. It is realized, now, that a number of the earlier patients were given inadequate irradiation therapy. During the last eight years or more, the patients treated by the combined method have been given some 3,000 to 4,500 mg. hours of radium preceding the hysterectomy. When the case was handled by irradiation therapy exclusively, 4,000 to 6,000 mg. hours of radium were administered. This dosage was obtained frequently by giving more than one treatment. The radium was applied in tandem, the number of capsules and the length of the applicator depending on the depth of the uterus.

Technical difficulties sometimes arise in the application of radium. It is applied into an invisible field of unknown dimensions. Sampson¹⁸ has shown that the sizes and shapes of the uterine cavities are quite varied, and that, frequently, it is difficult to irradiate uniformly a malignancy of the uterine body. Usually, the patient with a small uterus can be treated satisfactorily. The large uterus requires more radium, and there is a greater element of uncertainty in its application. Therefore, inadequate irradiation is more likely to occur. Regardless of these facts, irradiation therapy has a definite place in the treatment of the corpus cancer.

Preoperative irradiation is believed to be of definite value for five reasons: Preliminary irradiation should lessen the probability of dissemination of cancer cells at the time of surgery. It may destroy some malignant tissue even beyond the scope of the surgical extirpation. It definitely lessens the probability of contaminating the field of operation with carcinoma cells. It certainly decreases the likelihood of a local or a vaginal recurrence. Since the uterine wall serves as a distance screen to the parametrial structures, a larger dose of radium can be administered before the hysterectomy than can be applied safely in the vaginal vault. For these reasons, the probability of cure is enhanced by the use of radium, preoperatively. Apparently preliminary irradiation did not materially add to the difficulty of surgery. There have been seen no

appreciable detrimental results from its use. Vaginal recurrences were developed by three of the 14 cases, upon whom hysterectomies were performed, without preliminary irradiation (Fig. 3). This observation would seem to support the opinion that preoperative irradiation is of definite value.

When the uterus is moderately enlarged, due to malignant disease, there is probably an extension of the cancer to the parametrium, and these cases are



FIG. 3.—Vaginal recurrence four years after hysterectomy. No radiation therapy.

preferably treated by radium. However, when the enlargement is primarily due to fibroid tumors, since it is difficult to adequately irradiate such cases, these patients should have radium therapy followed by an hysterectomy. Considered as a group, the percentage of cures definitely diminishes as the size of the uterus increases. There were, in this series, ten cases who had markedly enlarged uteri, and apparently only two of the ten have been cured.

This review shows that ten patients were given irradiation therapy for a supposed benign lesion for a varying number of years preceding admission, the average being 7.7 years. Seven of these ten patients were admitted with advanced disease. This would suggest that cancer was probably present in some of the cases at the time of this previous irradiation treatment. It would also lend credence to the opinion that a number of these patients had abnormal endometria preceding the development of the corpus cancer.

It was the observation of Burnam¹ that there is a distinct tendency of these patients to develop cancer of an entirely different type in some other part of the body. Some observations noted in making this study would tend to support this point of view. There was one patient who had an adenocarcinoma of

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the fundus and, a year later, was found to have a squamous cell cancer of the cervix. Another patient had a mixed adenocarcinoma and squamous cell epithelioma of the fundus, and, a year later, she died of a sarcoma of the jejunum. Autopsy of this case revealed no evidence of a recurrence of the uterine cancer. Again, there was a patient who had a skin cancer and, five years later, adenocarcinoma of the corpus uteri, and still four years later, an

TABLE V
31 CASES TREATED BY IRRADIATION WITH
A FOLLOW-UP OF FIVE YEARS OR MORE

Survival	Number of patients
1 Year	5
2 Years	9
3 Years	3
4 Years	1
5 to 13 Years	13 or 41.9 %

TABLE VI
24 CASES TREATED BY PRELIMINARY
IRRADIATION AND SURGERY WITH A
FOLLOW-UP OF FIVE YEARS OR MORE

Survival	Number of patients
1 Year	2
2 Years	1
3 Years	1
4 Years	1
5 to 17 years	19 or 79.1%

early malignancy of the rectum. Another had a skin cancer at the time of the uterine malignancy. One patient had a breast removed for a malignancy two years before admission with the fundal cancer. Still another patient had two primary cancers of the fundus which had begun in separate polyps. One of these was a Grade I malignancy, and the other, Grade II.

CONCLUSIONS

The treatment of the patient with carcinoma of the fundus uteri should be individualized, for each case must be considered from several different points of view. The cardinal symptom of this pathologic entity is a small amount of irregular bleeding. There is only one accurate diagnostic procedure—biopsy of the uterine curettings. The majority of the carcinomata of the fundus have a malignancy of low degree of cell activity. The disease may remain local for many months or even a few years. There are three methods of treatment: Irradiation therapy; surgical extirpation; and a combination of these two methods. Proper irradiation therapy will cure a fair percentage of these patients, and this is the preferable treatment for approximately one-half of the patients with this pathologic entity. Improved technic in the application of radium may increase the percentage of patients to be treated by irradiation. Small doses of radium are inadequate. Added surgery to irradiation therapy definitely increases the probability of cure when the physical status of the patient is such that she is a good surgical risk. Surgical removal of the uterus following preliminary irradiation, in carefully selected cases, is a procedure carrying a very low mortality and gives, definitely, the highest percentage of cures.

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SECONDARY REPAIR OF CLEFT LIPS AND THEIR NASAL DEFORMITIES

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SECONDARY REPAIR of cleft lips and their nasal deformities may be required even though a good primary repair in infancy has been obtained, and there is little reason for anyone going through life with a noticeable deformity without having some attempt made for its correction.

Prevention of Deformity.—This is aimed at in the primary operation by trying to obtain: (1) A good alar level and direction; (2) a good nostril floor; (3) a good nostril curve, that is—across the tip; (4) a straight columella; (5) a full lip border in advance of the lower lip; (6) a full vermilion without a “whistling deformity”; and (7) a flexion crease, if possible, across the lip (Fig. 1). It is desirable to have (1) a cupid’s bow, but not at the expense of deforming the vermilion border; (2) a philtrum—but this requires a straight line incision, and the best that can be expected is a scar somewhere in the region of the philtrum and with the possible sacrifice of a few millimeters of tissue. Tendencies are to get the lips too long, and, therefore, too narrow, so that the typical retruded lip deformity is produced. It is usually better to have a full or wide lip that is short than a narrow lip that is too long (Fig. 8). Definitely to be avoided are wide suture scars with their ugly “ladder” effect, as they simply never can be eliminated altogether; it would be better to risk having a wound open up rather than put in wide sutures (Figs. 2 and 3). The type of operation employed is not so important as the essentials to accomplish in tissue conservation and adjustment. Figure 1 shows the result of a modified Mirault procedure, with the preservation of a small triangular flap from the cleft side.

The Secondary Repair.—Both the lip and nose usually need correction and have to be considered together in the plan and at the time of operation. If possible, tissue already present is simply readjusted; this may require sliding flaps of mucosa from the buccal fornix to allow advancement of the lip (Fig. 4), and an osteoplastic operation upon the nose, with reconstruction of the lower lateral cartilages (Figs. 3, 5 and 6). But in extreme deformities, it should be determined if there will have to be a skin graft in the buccal fornix to loosen the lip from the maxilla; a flap from the lower lip to balance the proportion with the upper; and, for the nose, if a septal resection, a skin graft or a cartilage transplant will be needed. Where a number of these procedures will be necessary, their sequence should be planned carefully, and the

gross restorations completed first. Both the lip and the nose may be repaired at the same operation, as in Figures 3, 5, 6 and 7, but they are separated in the description.

One other thing of importance in the plan is the inclusion of the patient's own idea of what is necessary, even though he may dwell on some small part of the deformity that is minimal compared to other features of it.

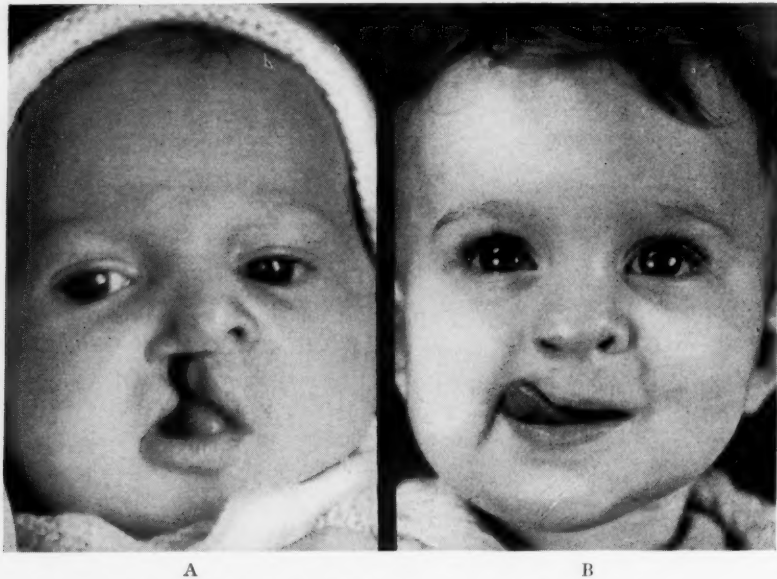


FIG. 1.—Cleft lip with bad distortion, shown one year after primary operation.

Although the operation has been planned beforehand, the final procedure often has to be figured out in the operating room, when the tissues have been opened and the possibilities of mobilization determined (Fig. 10). There is so much free-hand work that it is not possible to illustrate a standard procedure to be employed for every cleft lip repair. Instead, some of the essentials can be listed, and an effort is made to fulfill the requirements that have been mentioned above as ideal for primary repair.

Anesthesia.—This is usually obtained by novocain block of the infra-orbital and superior dental nerves, and by a small infiltration around the columella, but intratracheal ether is sometimes advisable.

Incisions.—These are carried along the previous ones, opening as few new areas as possible; the farther lateral the opening is made, the narrower and longer the lip will be after the new closure. Incisions inside may have to be carried far lateral in the fornix, to allow for advancement of the lip (Fig. 4).

The Readjustment.—This can be started with sutures at the vermillion border and the floor of the nose, as these points are good places to match the two sides; the location of these points is marked with 3 per cent methylene blue, using a fine, mechanical drawing pen.

If the lip and nostril floor have been opened, the floor is closed with a

REPAIR OF CLEFT LIPS

deep suture of chromic catgut to give strength, placed in the muscle and tied on the inside. Then, usually, a fine No. 000 white silk is placed close to the vermillion border. Fine skin sutures of No. 000 black silk are then used, or other material as desired, and, although they may pierce fairly deeply, they should *not* be placed widely. An effort is made to imbricate the vermillion border to avoid a notching or "whistling deformity" (Fig. 2). It might seem

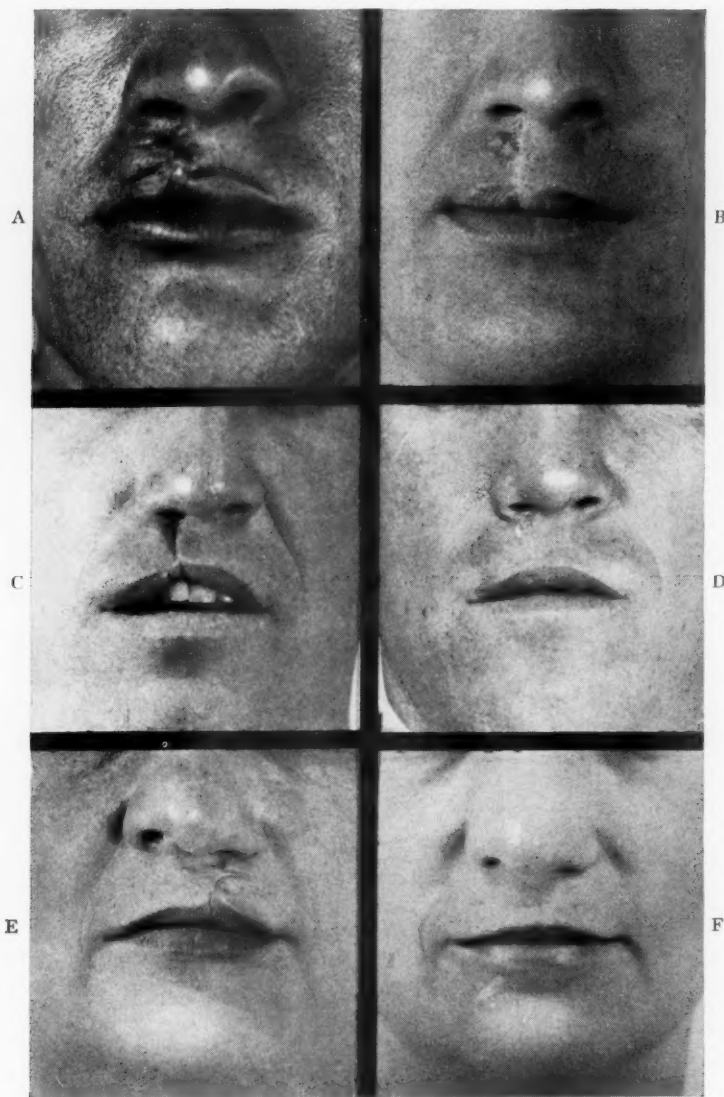


FIG. 2.—(A), (B) Suture scars from primary operation that leave their mark even after the second correction. (C), (D) Results of not carrying original operation far enough out into vermillion with secondary correction. (E), (F) Uneven vermillion, scars and "slumped" nose. Corrected in one operation on lip and a reconstruction of the lower lateral cartilage from the inside of the nose.

desirable to use one-half of the necessary amount from one side and one-half from the other, but it is probably best to get out into good thick vermilion as it is difficult to prevent the redevelopment of a notch.

The sutures on the skin surface are carried on very fine needles, and the skin edges are supported with fingers instead of forceps, whenever possible, to avoid scratching. The forceps used are fine ones, or an atraumatic type



FIG. 3.—Complete osteoplastic operation upon nose as main part of correction—no external nasal incisions. Stay-suture marks from first operation are present out on the cheeks.

with eight teeth running up the shank instead of across the end.¹ Fine hooks are preferred by some.

Construction of a Philtrum and Cupid's Bow.—As the philtrum and the vermilion border, where the skin shades into mucosa, are soft, delicate molds of tissue, it is difficult to conceive of actually reconstructing them by an operative procedure which leaves a scar in the area; no lip scar is as soft as a normal vermilion border and, although a scar down the lip may look something like a philtrum, it is just the substitution of a scar for a normal soft undulation in the tissue. It usually is not necessary to create a cupid's

REPAIR OF CLEFT LIPS

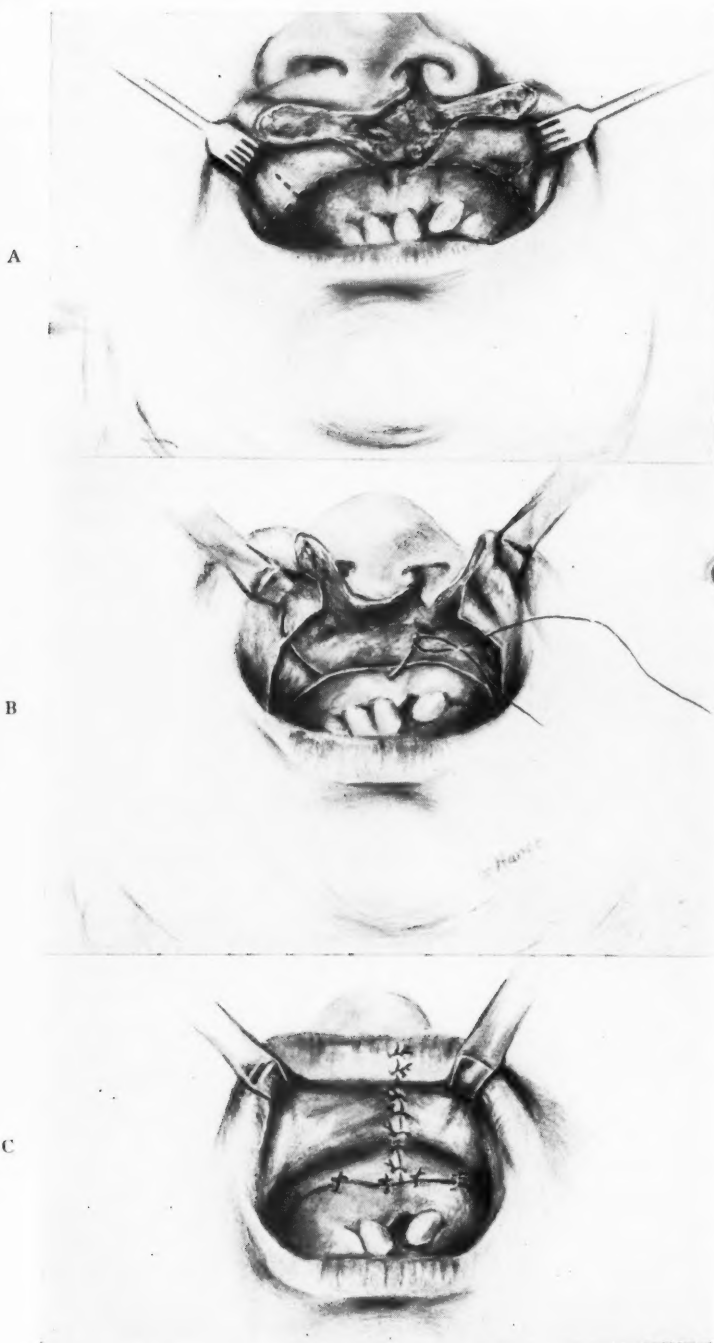


FIG. 4.—*Advancing the Lip to Free It from Alveolus:* (A) Lateral incisions carried far out in buccal fornix to free lip from adherence to alveolus. A short incision is made at a right angle to further ease tension. (B) One main suture on each side does most of the fixation in the new, advanced position, starting at the midline on the alveolus and picking up the lip mucosa several centimeters lateral. (C) With the mucosa advanced, there is an excess shifted to midline, so that closure can be made with restoration of depth to the fornix and, therefore, freedom of the lip from the alveolus.

how at the expense of losing the normal soft border—or to make a philtrum at the expense of sacrificing several millimeters of tissue.

A fault seen frequently is a Mirault flap (or triangular flap from one side) that is too large; this is due, usually, to having applied some standard rule of design at the first operation rather than fitting the design of closure to the available tissue (Fig. 8). For this deformity, a limited procedure sometimes can be carried out by simply reducing the size of the flap—but even this may require complete opening of the lip.



FIG. 5.—Nose and lip corrected in one operation, with no external nasal incisions and with reconstruction of lower lateral cartilage.

A serious fault is the occurrence of vermillion up in the surface of the lip; this has to be excised and sacrifices width and adds length—which is an undesirable situation because it further unbalances the proportions of the two lips (Fig. 8).

After the lip has been repaired and advanced, it has to be held there and, unless the upper jaw is far enough forward itself, a *dental prosthesis* to hold it out may have to be made. In badly deformed palates and upper jaws, this plate can be built over existing teeth as they may help the plate hold the lip forward (Figs. 9 and 11).

Free Skin Grafts in the Upper Fornix.—These are used if there is not enough mucosa to separate the lip from the bone, but they are not ideal, as there is often some tightening around the edge of the grafts that interferes with a good result.

Double Clefts.—These give about twice as much trouble as single ones,

and the possibilities of decent appearance are not even one-half as good. Where the *prolabium* has been used as full length of the lip, there is practically always an ugly deformity that requires advancement and filling of the large, resultant notch. Almost this same thing occurs if, at the first operation, the operator has not gone out into the full thickness of the vermillion the same as in single clefts (Fig. 10).

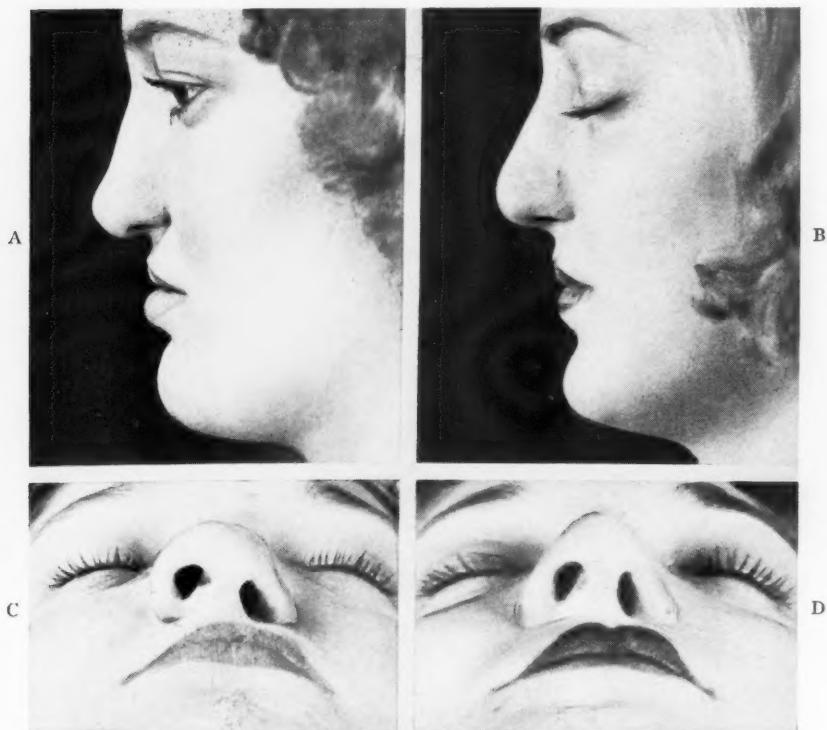


FIG. 6.—Nasal correction main part of work but the turn toward the septum is not made because the ala goes into the face so abruptly following the first operation.

Vermilion-bordered Flaps from the Lower Lip (Abbe or Estlander Flaps). —The repair of the above situation, and likewise where too much lip has been sacrificed or where too much scar has to be removed, often requires the use of a flap from the lower lip, as shown in Figures 9 and 11. This adds a scar to the lower lip, and the patch in the upper is an inert mass, often with poor color—but there may be nothing else to do when there is marked disproportion in the two lips. This flap may be almost any shape—rectangular, oval, or pointed—to go toward one or both nostril floors. Another use for the flap is in the occasional patient who has been unfortunate enough to have had the *premaxilla* and *prolabium* completely discarded at the first operation. This occurs, of course, only in double clefts, and is the expression of utter

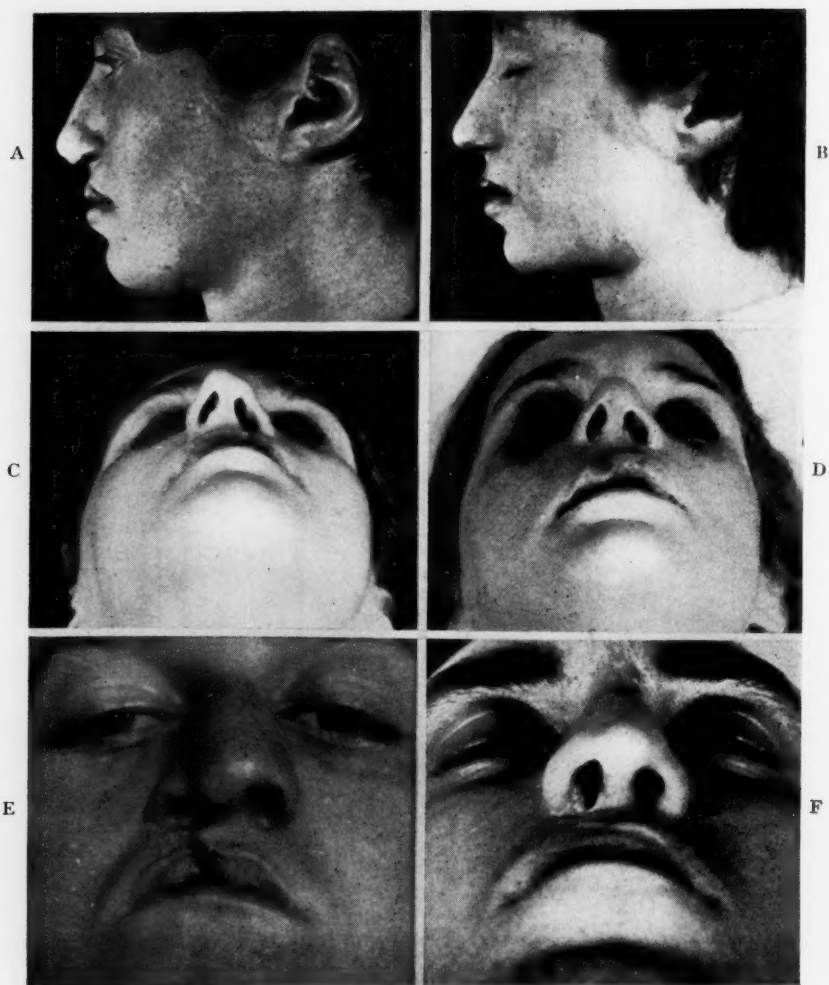


FIG. 7.—(A), (B) and (C), (D) Marked nasal distortions corrected by reconstruction of the lower lateral cartilages, without external incisions. (E), (F) Such marked droop of skin leaving so much excess that a full-thickness triangle has been excised from just above the border.



FIG. 8.—(A) Shows common failures that may occur in early repairs. The lip is too long and, therefore, too narrow; vermilion left in lip in two large patches. Mirault flap too large. Suture scars that are permanent. (B) Only repair possible without use of flap from lower lip.

REPAIR OF CLEFT LIPS

futility in trying to deal with the markedly protruded premaxilla and prolabium, as shown in Figure 12.

A tendency to forward protrusion of the lower jaw often occurs in these patients, and, along with this, there may be a marked active droop of the lower lip or such a marked effort to hold it up that it seems hypertrophied.

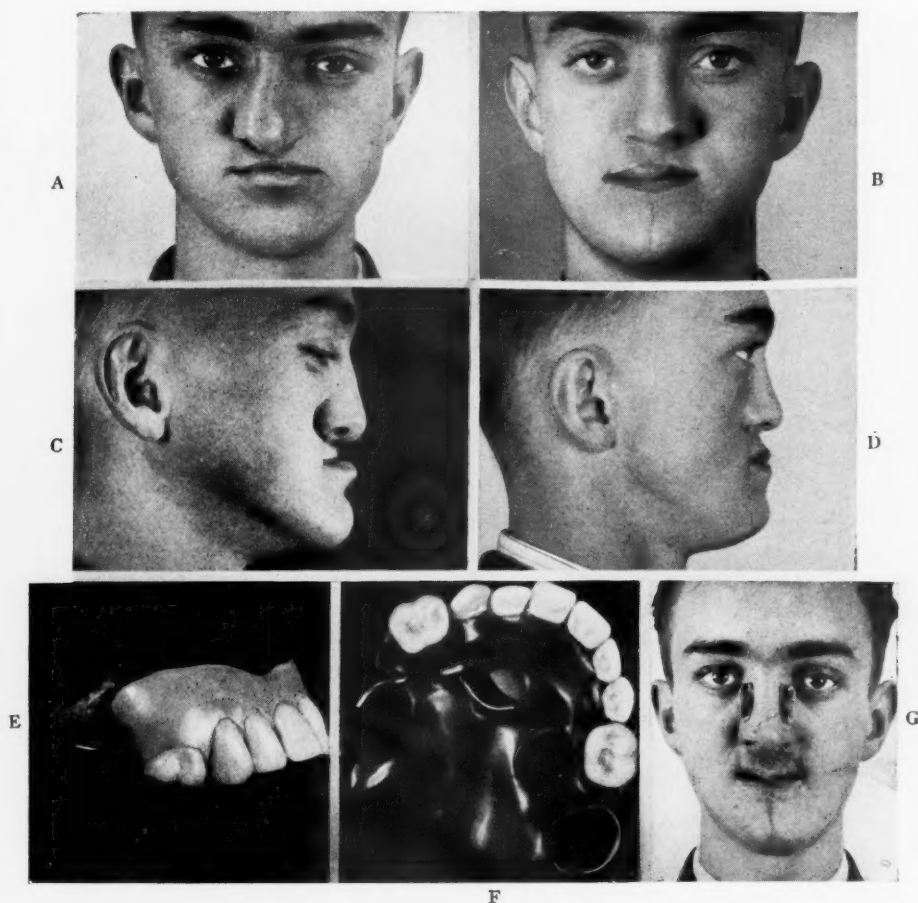


FIG. 9.—Patient with almost a "total" deformity, retrusion of upper dental arch and entire section of face. Marked elongation of nose, chin and overhang of lower lip.

Repair consisted of (1) complete osteoplastic operation upon nose; with (2) resection of triangle of bone from left side; (3) total reconstruction of lower lateral cartilages with *no* external nasal excisions; (4) advancement of cheeks on jaws; (5) lower lip flap to upper; (6) resection of prominent portion of chin; and (7) dental prosthesis made, by J. A. Brown, to fit over existing teeth.

This lower lip redundancy, producing further disproportion between the two, may be one of the most noticeable parts of the deformity. In correcting this, the use of part of the hanging lower lip for the upper lip is specific; if it is not needed there, a section may have to be removed from the lower, either as a full-thickness triangle or as an ellipse inside in the mucosa (Fig. 9).

Resection of the lower jaw or, preferably, reduction in the size of the

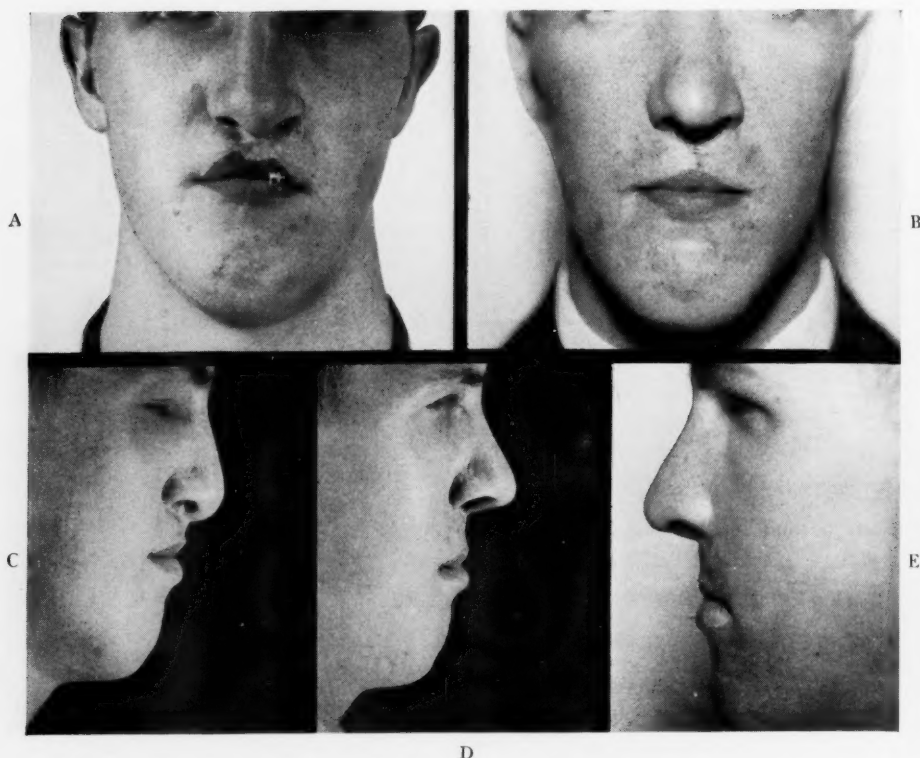


FIG. 10.—Secondary lip repair performed, with marked advancement along the buccal fornix and advancement of central part of lip into columella. Decision as to use of a lower lip flap made in operating room after it was determined how tissues would open. Resection of a portion of chin not undertaken because of excessive length of face throughout. The new columella was made firmer and straighter with a small, fresh homotransplant of cartilage.

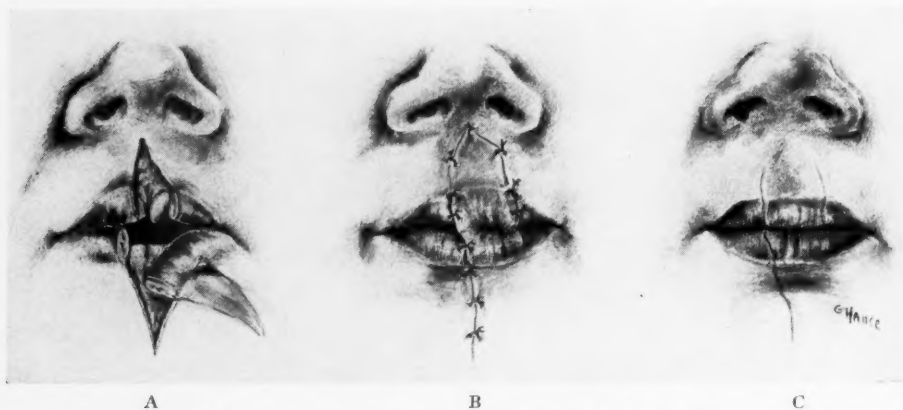


FIG. 11.—Diagram of Lower Lip Flap to Restore Proportion: (A) Flap removed from lower lip. This is triangular in shape to allow for closure. The part that is used can be cut to fit the upper lip defect to go around the ala, or to fit into one or both nostril floors. (B) Flap in place with pedicle containing inferior labial artery which makes the operation possible. (C) Pedicle cut after 10 to 20 days, and secondary adjustment effected of the vermillion border.

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chin may be undertaken if there has been a marked failure of growth with shortening as well as retrusion of the middle one-third of the face and of the nose (Fig. 9).

The Upper Dental Arch.—This has always presented a problem, if there has been a wide palate cleft, and although little can be done with the first teeth, as a rule, the second set may be greatly improved at times by orthodontia. One trouble is that the teeth may be far misplaced, very crooked, and have very poor bone support, so that the usual settlement is a small

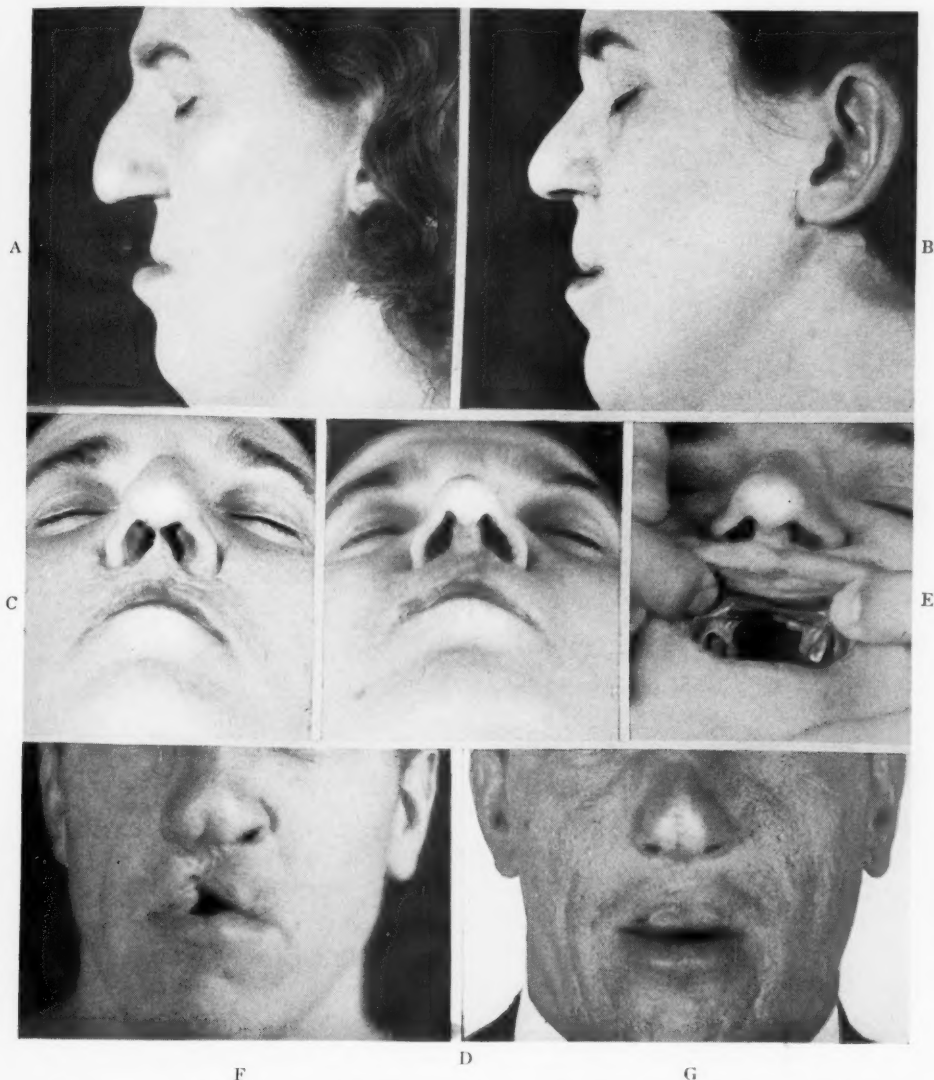


FIG. 12.—Loss of Premaxilla and Prolabium: (A), (B), (C), (D), (E) Restoration of columella by utilizing local tissue and dropping tip of nose down, so that the use of a distant flap was avoided. Lip held out with prosthesis, but lower lip flap might still be used. (F), (G) Total loss of prolabium and premaxilla partly corrected by wide undermining and advancement.

partial plate or bridge. The closer the arch is to normal, of course, the better speech will be.

REPAIR OF NASAL DEFORMITY

There are certain molds, skin folds, borders, and delicate shadings of the normal nose, lip, and mouth that seem to be the inalienable rights of nature—and they seldom are completely duplicated. We may strive for the best possible substitution and, in doing so, should make as few external scars as possible and sacrifice practically no tissue.

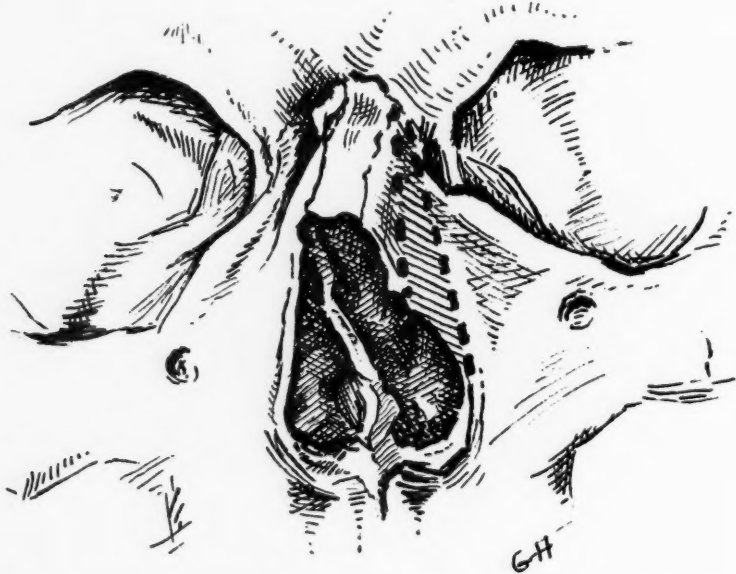


FIG. 13.—Resection of a Triangle of Bone from the Long Cleft Side of Nose: This is accomplished with saws from the inside, when the entire bony nose has to be shifted to the cleft side and when this side is too greatly out of proportion with the opposite side.

A good premise to follow is to try to repair these deformities by a regular osteoplastic procedure for the reduction in size of a nose, and to try to obtain an acceptable alar level and curve by a reconstruction of the lower lateral cartilage without making any external incisions. This may not always give complete forward correction of the nostril tip but, if the level and curve are close to normal, it may be left backward a little without being too noticeable. This avoids a correction with a full-thickness excision of skin or an attempted rotation of the nostril, which leave external scars on the ala and columella and may turn bivrissae out of the nostril in a displeasing fashion. But, occasionally, when the nose has been "slumped," elongated, and out of place for a long period, there may be so much excess skin over the alar region that some of it has to be removed by an external excision (Fig. 7 D and E).

When the nasal osteoplastic operation is used, the component parts of it are carried out as needed, starting with a removal of a dorsal hump, nar-

REPAIR OF CLEFT LIPS

rowing the side walls, and straightening the septum. This is essentially a Joseph operation, and has been employed in the patients shown in Figures 2, 3, 5, 6, 7 and 9. When the lateral bony walls are very much deviated, a triangle of bone may have to be taken out of one side to allow for the same final proportion on the two sides, as shown in Figure 13. Also, a badly

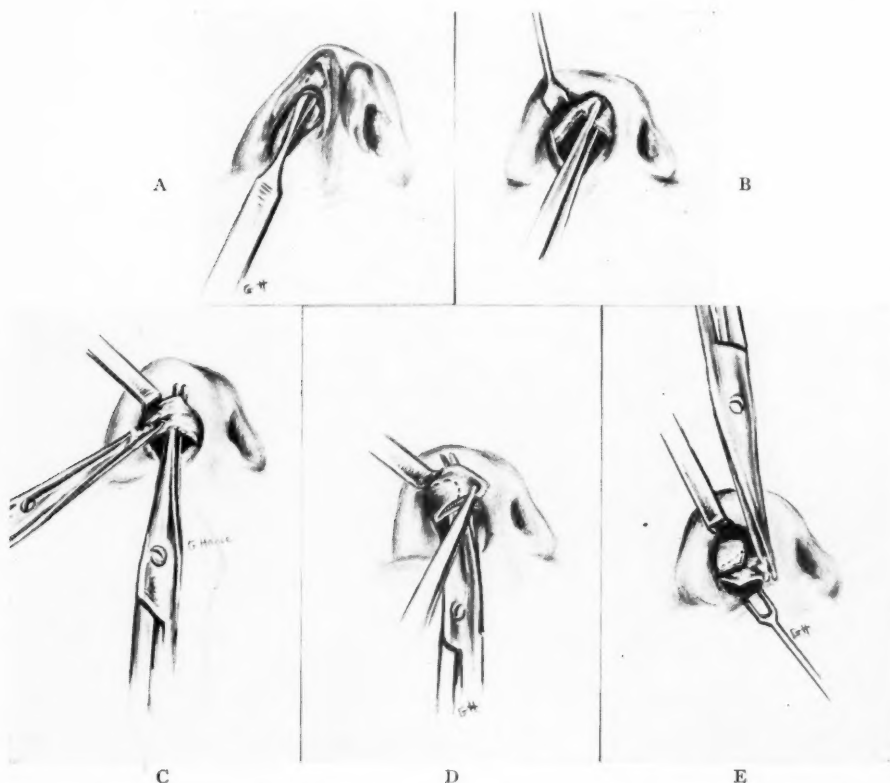


FIG. 14.—*Reconstruction of the Lower Lateral Cartilage:* (A) Incision around lateral and medial crus just inside border. The upper border is freed by a separate incision between the upper and lower lateral cartilages. (B) Dome of cartilage grasped with forceps and drawn down out of nose, being left attached medially and laterally. (C) Loose tissue dissected free of cartilage to completely expose it and to avoid thickening after operation. (D) Trimming away excess cartilage in dome and from upper border. (E) Trimming lower edge of cartilage to give new direction to tip and further prevent the hanging appearance.

deviated septum and nasal spine may have to be loosened and swung over as a trap-door and, if necessary, wired to a tooth with a mattress of silver wire.

Reconstruction of the Lower Lateral Cartilage.—This is the most important part of the correction, and is carried out as in any complete nasal plastic operation, but with more attention and work on the affected side, and it is important that the sound side usually has to be done also. This is accomplished by a wide freeing of the cartilage, so that it can be brought down out of the nostril, visualized, and trimmed as shown in the drawings (Fig. 14). Part of the dome of the alar cartilage may be turned up to make more of a medial crus, or the lateral crus may be brought over and anchored to the

opposite cartilage up over its own medial crus. This plan has been used in the patients in Figures 2, 3, 5, 6, 7 and 9.

Direction of the Ala.—The direction, as it comes into the face, is important, and it should turn toward the nose but, if the primary operation has left it a stocky mass going into the face at a right angle, little can be done about this direction without more objectionable external incisions (Fig. 6).

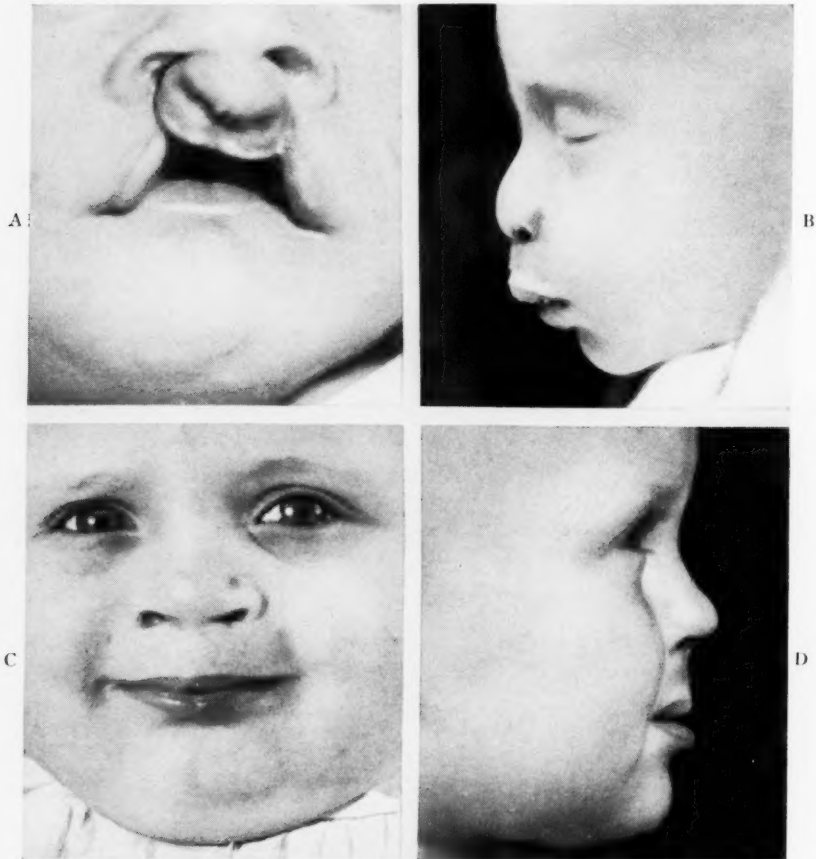


FIG. 15.—(A), (B) Complete double cleft lip with immediate correction. (C) Result one year later, with no sign of columella. (D) Result of advancement of a columella from the lip at three years of age.

Floor of the Nostril.—This is worst when inadequate or depressed so that the nostril can be seen into too easily and too far. This can usually be corrected by local mobilization of tissue but may require a triangle taken from the cheek just around the curve of the alae. This same restoration can sometimes be used for a nasal floor that is too high when the alae are pulled far up on the septum.

Intranasal Correction.—This consists mostly of getting rid of or straightening septa that are blocking airways, and may be done at the same time, or later, as a separate step if desired. Completely blocked nostrils are usually

REPAIR OF CLEFT LIPS

very difficult to restore and require free skin grafts after very careful opening dissection.

Secondary Nasal Corrections in Double Clefts.—These corrections, as in the lip deformities, are twice as difficult and results are about one-half as good

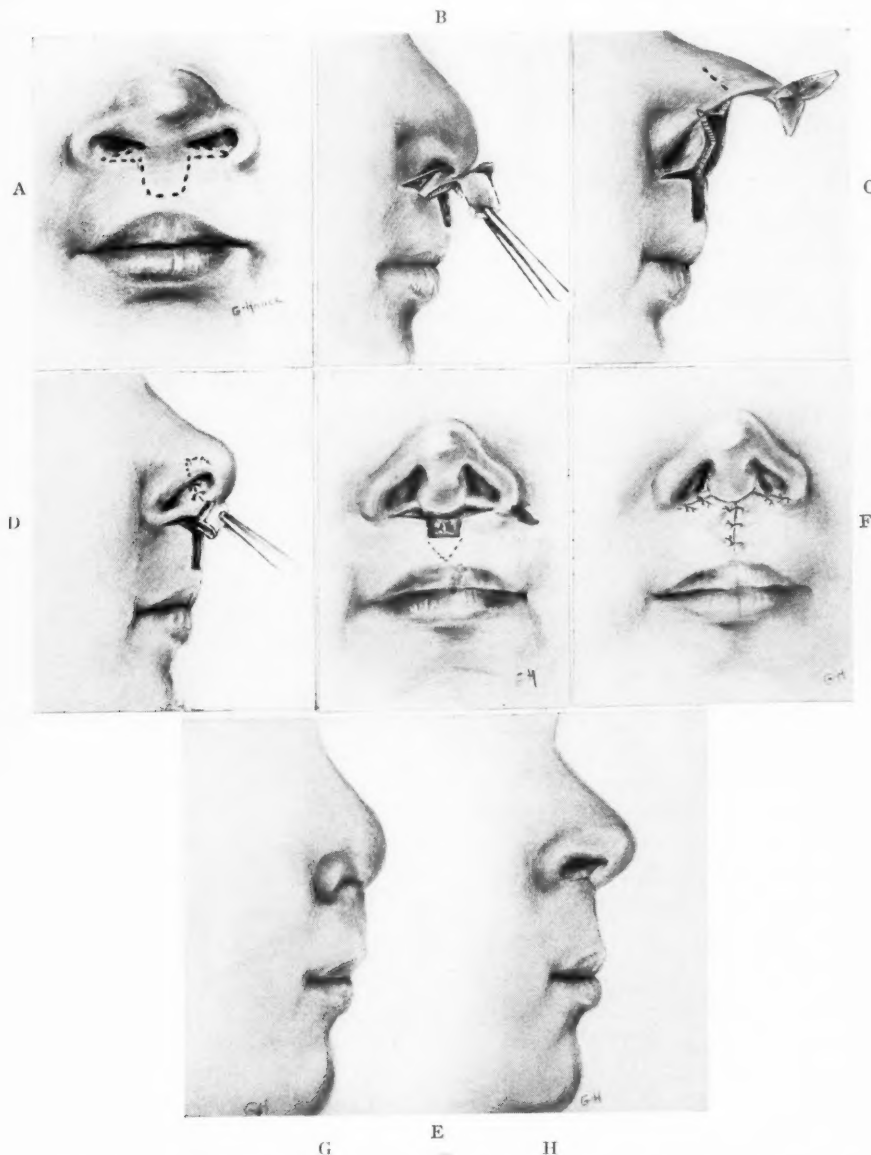


FIG. 16.—Columella Construction by Advancement of Flap from Lower Lip: (A) Design of continuous flap, with base at tip of nose, lateral triangles to fill opening in septum and to allow for shortening of lip. (B) Flap dissected free. (C) Tip and dorsum of nose loosened and freed from septum by incision up over top of septum. (D) Flap being sutured in place, with full extent going along base of septum and small triangles from floor of nose going in along both sides just above septum. (E) Flap in desired position at a right angle to lip, and not pulled back down in it. (F) Lip closed by shifting it clear over to midline without putting sutures in new columella that will drag it back down in lip. (G), (H) Profile before and after advancement of lip flap for columella.

as in single clefts. The *columella* is constructed by advancing part of the prolabium from the lip into a position below the septum after the entire area over the tip has been freed and the membranous septum has been incised. Cuts into the mucosa high up over the septum are made, which open up in little "darts" and allow elevation of the tip. Into these little triangles, small "darts" that have been raised from the floor of the nose and have been left attached to the prolabium can be placed. One necessity is that the new columella should make practically a right angle with the lip, and care has to be taken that the elevated prolabium is not sutured back down in the lip with the production of an ugly web (Figs. 10, 15 and 16).

It is a question whether the prolabium belongs to the columella or lip, but when it is observed that the columella, made this way in a male, has to be shaved, then the argument must be in favor of the lip. Occasionally, the newly formed columella retracts too far into the nose and, if so, about the only correction worth while is to perform a *costal cartilage implantation*. The patient in Figure 10 shows about as normal a columella in size and shape as can be obtained in double lip clefts, and it was made by advancing part of the lip up along the base of the septum at a right angle to the lip, and later putting in a small cartilage transplant.

There is a tendency to elongation of the lip and collapse of the nostrils by this procedure; the elongation can be helped some by the slight elevation afforded by closing the floors of the nostrils from where the triangles have been taken. But the reapproximation of the two sides of the lip may be very difficult and require careful lateral freeing. Otherwise, there is a tendency to pull the prolabium back down in the lip and leave the web mentioned above (Figs. 15 and 16).

The columella may be impossible to obtain from the lip and an *arm- or wrist-flap* may be required. However, every effort should be exhausted to use local tissue, as shown in Figure 12, before resorting to the arm-flap.

Where the *premaxilla* has been jammed or crushed backward at early operations, there is almost sure to be an occluded air-way on one side. This may be dealt with by excision of the mass, but skin grafting may be necessary to restore the nostril opening. Occasionally, the premaxilla may remain in such a peculiar forward position that a right angle has to be chiseled into it to permit of a final right angle at the columellar lip junction.

The surgeon may be called upon to help decide in the adjustment of these patients in regard to their *social, educational, economic, and marital status*.

The repaired nose and lip are not perfect and, therefore, as little attention should be called to the face as possible. For this reason, the patient should be well modulated in all his reactions and in his speech, tone and loudness of voice. He should avoid forwardness of any kind, and facial grimaces should be abandoned to the point of becoming a retiring sort of person. Speech defects are made worse by a poor muscle function of the lip, and voice modulation is still more important for this reason.

As to livelihood, persons with speech defects or scarred lips should adopt

work or professions where they do not have to give or receive advice too often or where they do not have to appear conspicuously in the public eye. It is gratifying that many of these patients are exceptionally intelligent and progress in school better than average, and the age-old idea that persons with cleft lips and palates are stigmatized in any way is wrong. *Marriage* and *heredity* are important points that have to be met very often. These patients are more apt to have children with clefts than if they did not have a cleft themselves, but many prove to be ideally suited for family life and have children without clefts.

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WHY INGUINAL HERNIA RECURS

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THE PERSISTENTLY HIGH RATE of recurrence following operations for the cure of inguinal hernia, particularly the direct variety, would suggest that there must be something inherently wrong in our method of dealing with it. In very recent years there has been a marked improvement in the reported results, particularly those in which the fascial suture is employed.

The object of this paper is to establish the reason for recurrence, and how it may be overcome.

When Bassini² began his studies of inguinal hernia he was intrigued by the fact that the testicle, which is originally an abdominal organ, descended into the scrotum through the inguinal canal, having been preceded by the processus vaginalis. His theory was that this left a weak route that either persisted, resulting in a congenital hernia or was easily entered subsequently, resulting in the indirect hernia. There is no question of the value of his observations or about the value of his operation in curing hernia. He describes the principle of his operation as follows: "In both cases, that is in external (acquired or congenital), or in internal (direct) herniae, the inguinal canal is reconstructed after the manner of its physiologic formation, that is, with an abdominal and superficial opening, of which the first lies external to the second; and is provided with two walls, one posterior and the other anterior. Under the influence of abdominal pressure, the new posterior wall is pressed against the anterior and both support each other to withstand the continuous and strong impulse of the abdominal viscera, while the spermatic cord is permitted to pass through between them. The new abdominal opening and the new posterior wall of the inguinal canal are formed from muscular and aponeurotic tissues which functionate and, therefore, cannot disappear by resorption."

However, he did not go far enough. It remained for the Hopkins' group (Halsted⁶ and Bloodgood³), to discover that in direct hernia there was an actual muscle deficiency, so that by invaginating the scrotum and following the cord the finger would pass over the superior surface of the pubic bone and, in direct contact with it, into the abdominal cavity.

It follows, quite clearly, that constructing a new inguinal canal cannot possibly cure direct hernia, because the direct hernia occurs at the lower end of the inguinal canal. The various modifications of the Bassini² operation have likewise not been adequate.

Halsted,⁶ Bloodgood,³ and Downs,⁴ all described an operation which consisted of securing a flap from the rectus sheath, but they all found this opera-

tion unsatisfactory and abandoned it; and Downs⁵ states: "The problem of inguinal hernia resolves itself into the management of the direct variety. I have personally reached the conclusion that a certain number of direct herniae cannot be cured by operation."

Bloodgood³ states: "The chief cause of recurrence in the lower angle of the wound, stated in a previous report of operations at Johns Hopkins Hos-

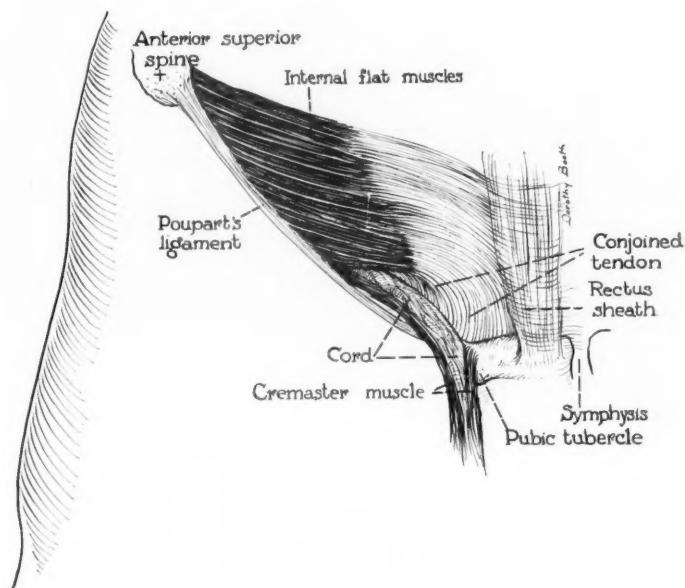


FIG. 1.—Normal musculature of inguinal region.

pital, in 1899, was due to the fact that, whether the hernia was direct or indirect, the conjoined tendon was weak or obliterated, and the ordinary suture or closure of the defect in the abdominal wall was not sufficiently strong to protect from recurrence in the lower angle, and that the transplantation of the rectus muscle and its fascia was not a certain cure."

A study of this area of muscular deficiency will explain several most interesting problems which must be overcome if cure is to be effected.

In the first place, there is a muscular deficiency which can and should be demonstrated at the time of operation (Figs. 2 and 3). Normally, the lower segment of the internal flat muscle arises from the outer two-thirds of the inguinal ligament, anterior to the cord and the abdominal ring, snugly encircles the cord, and is inserted as the conjoined tendon behind the superficial ring into the crest of the pubes and the iliopectineal line (Fig. 1). In direct inguinal hernia this portion of the muscle is absent to a variable degree, leaving the entire inguinal canal with an inadequate mechanism for closure (Fig. 3). I do not mean to say that we do not have congenital and indirect herniae when there is no such defect present, but I do say that, when the defect is present, we are likely to have direct and indirect herniae. This explains why

it is that, so frequently, direct and indirect inguinal herniae occur in the same individual. The shutter-action of the normal muscle, described by Sir Arthur Keith,⁸ not only keeps the canal closed but, undoubtedly, I think assists in the obliteration of the processus vaginalis (Figs. 4 and 5).

When the muscular deficiency can be demonstrated by invagination of the scrotum, as explained, we find, on dissection, that the lower segment of the

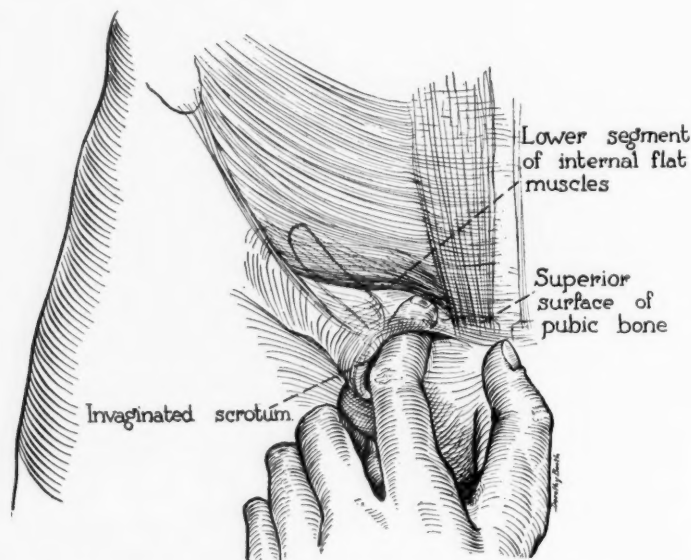


FIG. 2.—Method of testing integrity of lower segment of internal flat muscles. By invaginating scrotum, the finger passes over the cord in immediate contact with the superior surface of the pubic bone and into the abdominal cavity.

internal flat muscles passes directly over to the sheath of the rectus where it is inserted with its lower margin a variable distance above the pubic bone (Fig. 5). We have, then, this space which may be filled in with the transversalis fascia, but even this fascia may be absent or very attenuated, in which case the opening is closed only by peritoneum. The base of this irregularly triangular area is formed by the smooth superior surface of the pubic bone (Fig. 5).

If the lower segment of the internal flat muscles is sutured only to the inguinal ligament, as is the usual case, it at once becomes apparent that there is a space left above the smooth surface of the pubic bone, to which nothing is attached, and the space is not obliterated. It is because this space is left unprotected, as operations are ordinarily described and performed, that operation for direct inguinal hernia is so often followed by prompt recurrence (Fig. 8).

Also, as there is a defect to be closed, it follows that suture must be applied under tension. For this reason, if the sutures are of nonabsorbable material they will cut out; if absorbable sutures are used they will absorb and the sutured tissues will have a tendency to spring apart. In addition, ordinary

RECURRENT HERNIAE

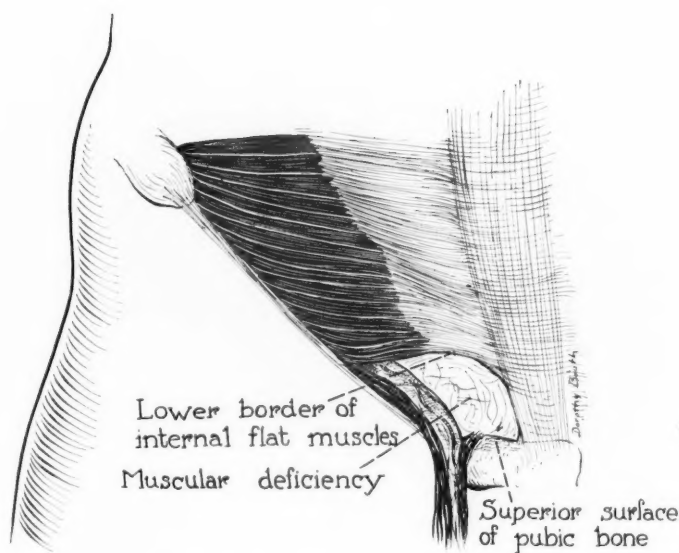


FIG. 3.—When the finger passes into the cavity as described, it means that there is a muscular deficiency and the conjoined tendon is absent. At operation, we find the condition above, the lower segment of the muscle passing directly over to the sheath of the rectus.

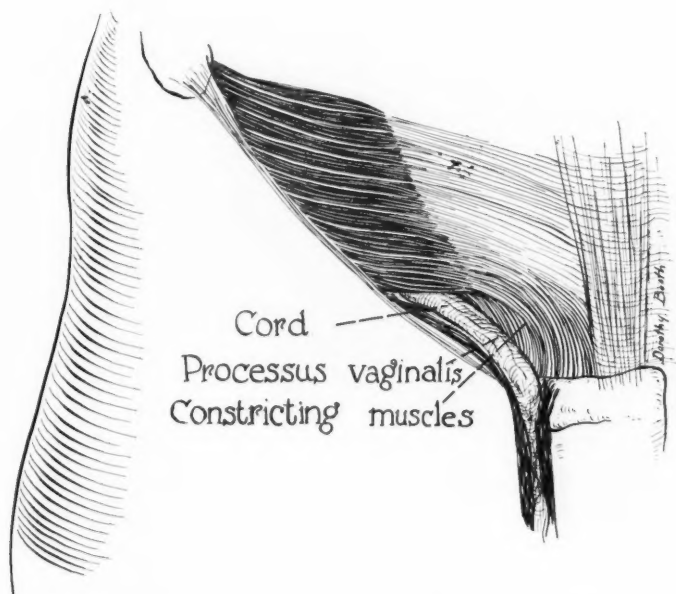


FIG. 4.—This drawing shows the normal relation of the lower segment of the muscles to the cord. The muscles arise in front of the cord, pass over it, and are inserted as the conjoined tendon behind the cord. Contraction of this muscle produces the shutter-action, i.e., it closes the inguinal canal. The processus normally becomes obliterated, and this is no doubt aided by the contraction of the muscle. If the processus persists we have a congenital indirect hernia.

sutures only approximate the edges of the structures sutured, and the strength of the suture line depends upon the adhesions that take place between the sutured structures. As the edges are often attenuated, the suture line is liable to be weak (Fig. 7).

Reference has been made to the improved statistics for hernia operations, where fascia is employed for suture. Bearing out this statement, Joyce,⁷ of

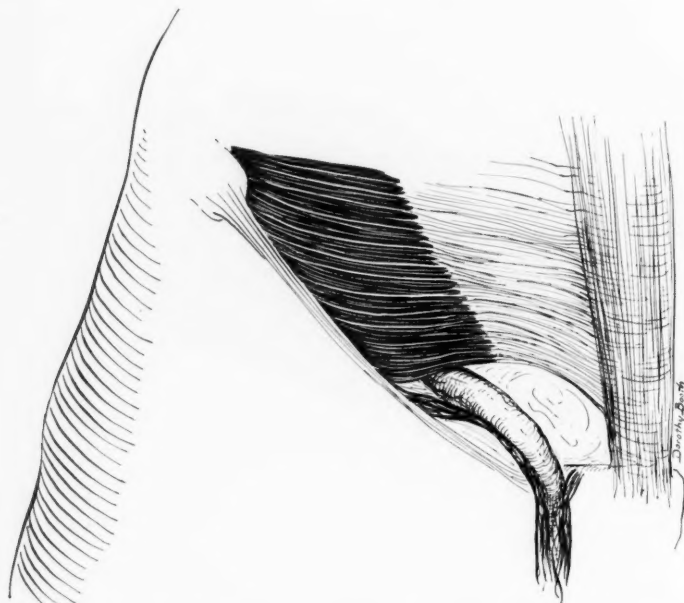


FIG. 5.—When the lower segment of the muscle is deficient, the muscle does not pass around the cord and the processus, as in Figure 4, and there is no shutter-action. Consequently, there is more likely to be a congenital hernia or indirect hernia.

Portland, Ore., in his Chairman's Address at the 1940 meeting of the A.M.A., reported on the results of "Fascial Repair of Inguinal Hernia," in which he describes his own very ingenious operation. In a five-year period, 180 hernia repairs were performed, by himself and his associates, on 149 private patients, of which 124 were traced—with a recurrence of one, or 0.8 per cent.

In the collected cases, in whom the operation was performed by various members of the Staff and Residents, 760 operations were performed upon 674 patients, of which 544 were traced. Of this number, there were 16 recurrences, a percentage of 2.94 for all traced operations. Of this number, however, 13 recurred within ten months or less, and, of this number, four recurred in two months or less. I believe that these statistics will be hard to beat, but the early recurrence, usually, means that there is some weak spot in the operation. It is possible that if the fascial suture had commenced on the ligamentous covering of the pubic bone 13 of the recurrences would have been eliminated which would leave only three recurrences in 544 operations; which, for a large number of cases, would hold the World's record, I am sure.

RECURRENT HERNIAE

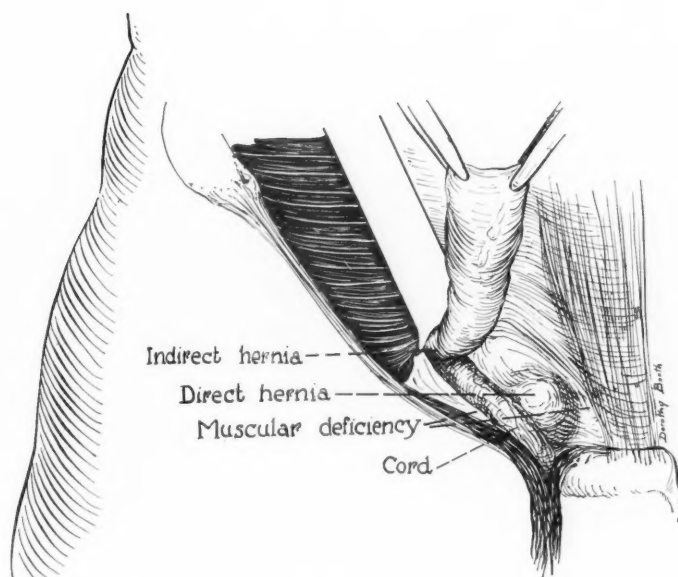


FIG. 6.—Shows both indirect and direct hernia in the same individual. This is a rather common occurrence and is, apparently, due to the same muscular deficiency.

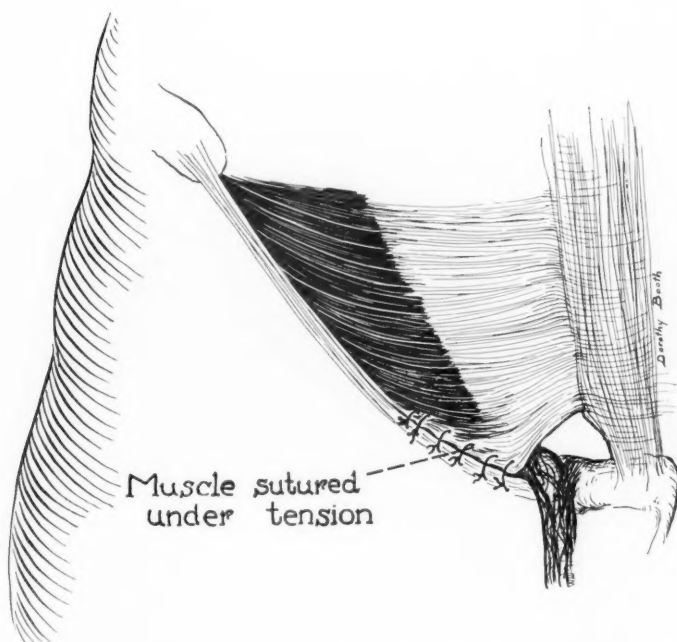


FIG. 7.—When sutures are of catgut, silk, cotton or wire, the most that can be done is approximation of the edges and this is done under tension. With catgut, absorption takes place and nonabsorbable sutures cut-out so that the defect has a marked tendency to recur. As the muscle is often attenuated, suture of the edge gives little support.



FIG. 8.—Bassini, and all others advocating similar types of operation, has laid so much stress on reconstructing an inguinal canal, that the real weak spot has been overlooked. This is the muscular deficiency which is most marked in the region of the superficial ring. It follows that the mere construction of an inguinal canal that does not take into consideration and overcome this essentially weak spot, if present, is going to be followed by a recurrence, more or less frequently, whether the hernia is direct, indirect or both.

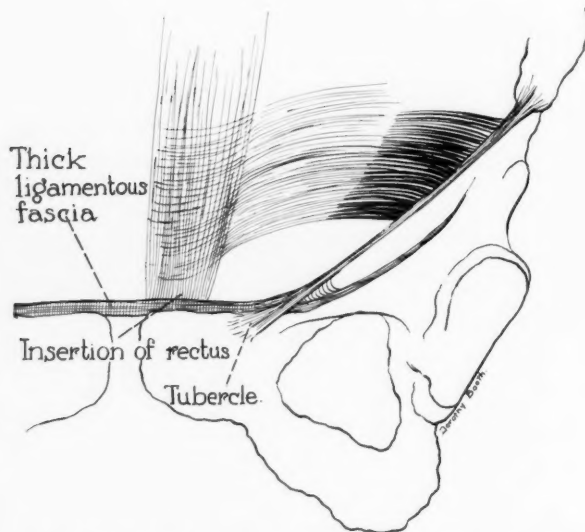


FIG. 9.—It does not appear to be generally known that there is a ligamentous covering of the superior surface of the pubic bone that is very tough, and so thick that the heavy fascial needle can take a bite in it without any risk of its tearing, or cutting-out. This covering is the key to the cure of hernia where the muscular deficiency exists.

RECURRENT HERNIAE

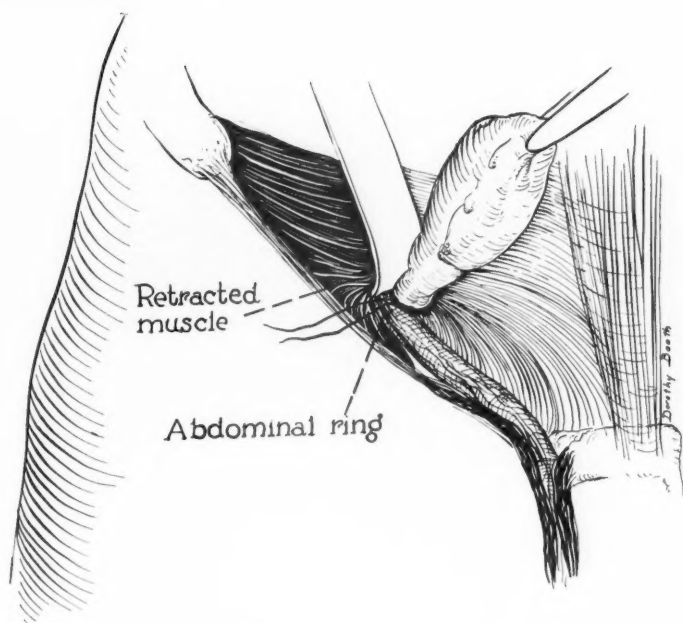


FIG. 10.—If the hernia is of the congenital or indirect type, and there is no muscular deficiency, the removal of the sac and its high ligation should be sufficient for a cure. After the sac has been removed, the normal action of the muscles is sufficient to protect the opening. There is a question if suturing does not impair the muscular action. The abdominal ring, normally, lies behind the internal flat muscles which have to be retracted to expose it. The normal lower segment of the internal flat muscles responds to, and closes the inguinal canal.

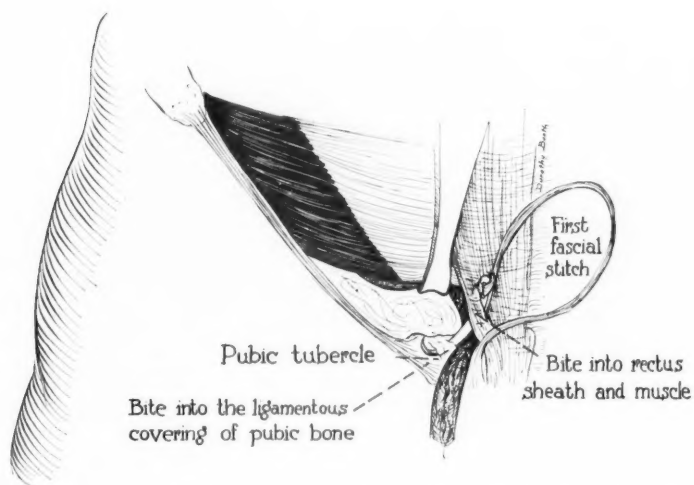


FIG. 11.—If hernia is to be cured, the cure must be directed to the weakest spot. This is where the muscles pass directly to the rectus sheath leaving a definite muscular defect. The first fascial suture should commence with the rectus muscle and sheath. The cord is retracted under the rectus muscle, and the suture is commenced at a point in the rectus sheath and muscle which will bring them snugly over the cord, and then take a bite in the thick ligamentous covering of the pubic bone. The exact point at which this bite is taken, depends on the extent of the opening to be closed.

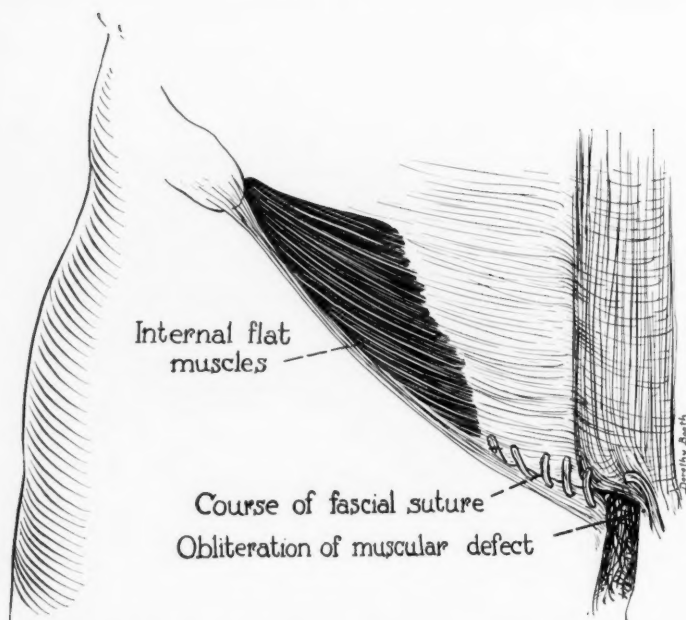


FIG. 12.—The stitch is continued outward suturing the rectus and then the border of the internal flat muscles to the pelvic bone—the tubercle; Gimbernat's; and Poupart's ligament. This forms a complete muscular shelf, all of which is anterior to the cord. If the fascial suture gives out, the suture can be completed with fine silk or chromic catgut. There is, usually, no particular strain at this point.

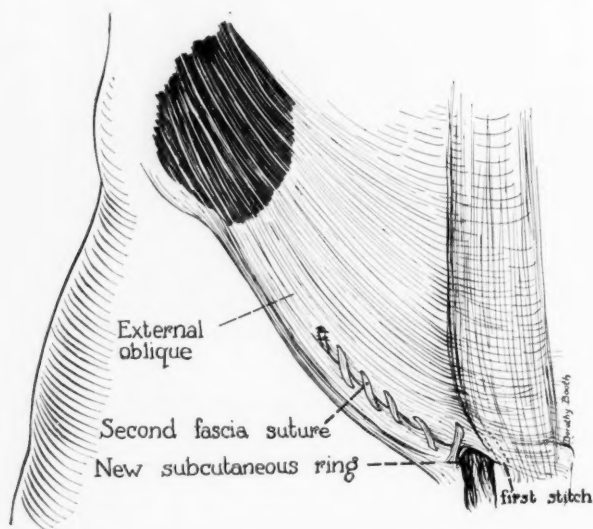


FIG. 13.—The fascial sutures are secured from the pillars of the subcutaneous ring, and are left attached at the pubic end. The first suture is placed as described. The second suture is employed to repair the fascia of the external oblique, which has been incised to expose the inguinal canal. The second suture is carried snugly over the cord to the opposite edge of the fascia, in such a way as to make a new subcutaneous ring. It, thus, gives a certain amount of support to the underlying tissue, and as the suture is fascia it will not stretch.

The prevention of recurrence of inguinal hernia involves the accurate diagnosis of the condition present, and the application of a technic that is adequate for overcoming the defect:

(1) The first step in all cases of inguinal hernia is the maneuver of invaginating the scrotum. In women, other means of making a diagnosis will have to be employed (Fig. 2).

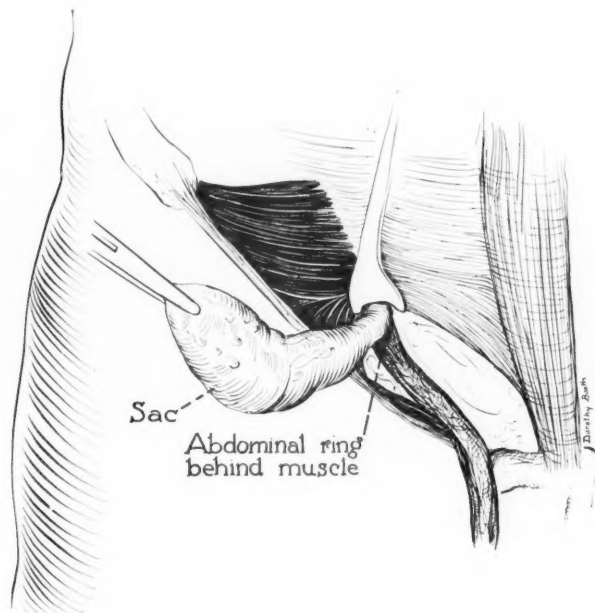


FIG. 14.—The cord is left undisturbed in its bed, except that a search should always be made for a possible indirect or congenital sac. This should be removed by an high ligation. The abdominal ring then drops back behind the muscle.

(2) The passage of the finger over the smooth surface of the pubic bone establishes a condition that has been difficult to overcome. In whatever way the tissues may be sutured, if this smooth surface is left as the base of a canal, recurrence is invited (Figs. 2 and 3).

(3) To Babcock¹ should be given the credit for the discovery that the superior surface of the pubic bone has a thick ligamentous covering that is several millimeters thick, which is densely adherent to the bone, and easily admits suture with the large fascial needles (Fig. 11).

(4) The problem is to cure the muscle deficiency. As stated, ordinary sutures have proven to be inadequate, because they are applied under tension. In any event, by these methods, only the edges are approximated, and when the muscular tissue is attenuated the suture link is weak (Fig. 8).

(5) By taking advantage of the ligamentous covering of the pubic bone, and using the McArthur⁹ fascial suture, the heavy rectus muscle and sheath can be permanently attached to the pubic bone, and continued outward, so as

to make an adequate barrier to any subsequent descent of the hernia. This fascial suture becomes incorporated in the muscle and fascia, and forms a permanent attachment to the pubic bone and to the other tissues to which it is sutured. We have, thus, the strongest tissues permanently applied to the weakest spot (Fig. 11).

We can, then, conclude that the cause for the recurrence of inguinal hernia is a muscular deficiency, which leaves an aperture that has been difficult to obliterate. However, by making use of the ligamentous covering of the superior surface of the pubic bone, and using the fascial suture, advocated by McArthur,⁹ this can be adequately accomplished.

The objects of this communication are to present, in outline, the principles involved in the recurrence of inguinal hernia. The technical details are clearly shown in the series of illustrations, and need not be repeated in the text.

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CHEMOTHERAPY AS AN AID IN THE MANAGEMENT OF ACUTE OSTEOMYELITIS

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ACUTE OSTEOMYELITIS develops as the result of a blood-borne infection, the pyogenic bacteria entering the blood stream from some focus. It is one of the serious diseases of childhood; first, because of the possibility of septicemia with a fatal termination in a high percentage of cases; second, because of the frequent and permanent crippling results; and third, because of the frequent long convalescence that may follow even with the most skillful medical and surgical management.

The infection may involve the flat bones but is more commonly seen in the long bones. The shaft of the long bone consists of the periosteum, compact and cancellous bone and the marrow, with the blood supply coming from the nutrient artery, periosteal and epiphyseal capillaries. The source of the infection must, necessarily, be the surface of the body, the upper respiratory tract or the alimentary canal. It may be difficult in certain instances to determine the source of infection, as many times the osteomyelitic process develops after the primary skin lesion has healed and the scar is not conspicuous. In some cases the bone lesion may be secondary to one of the exanthemata.

The primary source of infections listed in the series, has been found to be principally from the upper respiratory tract with the exception of two cases, one of these having a history of skin lesions, and the other an acute otitis media.

Cultures of the exudate from the local lesions gave growths of *Staphylococcus aureus* in all cases except five, four of which showed *Streptococcus haemolyticus*; in one case there was no culture recorded.

Clinical observations indicate that the virulence of the organism and the general physical condition of the child may influence the extent of the lesion. The history of a sick child with osteomyelitis often reveals the fact that there has been a preceding infection or debilitating disease. Faulty habits of eating predispose to malnutrition. The incidence of osteomyelitis during late years appears to be lower. This may be the result of an improved nutritional state among children of parents in the low financial brackets. The disease is most frequently seen among the poorer classes of city children, although it is also found in children living in the rural communities. A properly balanced diet with correct vitamin content is important and apparently has aided in lowering the incidence of the disease. The work of Nelson¹³ on bone metabolism has

led him to believe that normal bone is never infected and that a mineral imbalance probably precedes a bone disease. The public school system in Detroit has made it possible for children showing clinical evidence of malnutrition to receive supplementary feeding while at school. Possibly this is a factor in reducing the incidence of the disease in the Detroit area.

In this study, trauma has been found to be a possible factor in about 40 per cent of the cases and bears some relation to the initial area of bone involvement. The injury may be a direct blow or a twist of the extremity near a joint. Experiments and clinical research¹⁹ have demonstrated that slight trauma is sufficient to cause fractures of the delicate normal trabeculae of long bones followed by effusion, hemorrhage, and interference with nutrition. This develops a decreased resistance with a strong tendency for any available organism to localize. Starr,¹⁷ and his coworkers showed that the offending organism carried by the blood stream reaches the finer capillaries in the juxta-epiphyseal region of the long bone. If the general resistance of the individual has been lowered and the local resistance has been reduced by trauma, an infective process develops and a small inflammatory area in the cancellous bone near the epiphyseal line results. Wilensky¹⁸ concludes that the process is a thrombo-embolic phenomenon, with the development of a pathologic process which is characterized by a thrombo-arteritis or a thrombophlebitis and necrosis of the bone cell and tissue. It is apparent from his study of the anatomic, pathologic and clinical facts, that either the nutrient artery or one of its branches becomes occluded. This observation is further verified when the pathologic process is found to progress in spite of what is considered to be early adequate drainage at the site of the disease. In many instances, a destructive process of the whole or half of the diaphyseal shaft develops.

The clinical picture of early sepsis manifests itself with fever, although sometimes it may be initiated with a chill. The temperature may range from 102° to 104° F. and higher, and is associated with a rapid pulse, malaise, headache and sometimes vomiting. The child looks sick because of the overwhelming toxemia, dehydration and the loss of sleep, especially where the disease has been present for several days. Delirium, stupor, and even convulsive seizures may be observed. The laboratory findings are what would be expected in an acute infection.

Pain and inability to use the extremity involved are the outstanding subjective symptoms of osteomyelitis. This pain⁷ results from infection and inflammation of the periosteum and may be so severe that it can be aggravated by the vibrations created in the room by one walking near the bed. The pain is excruciating and the patient, if seen early, usually remembers the approximate time of the sudden discomfort. The outstanding objective finding is tenderness on percussion at the point of the disease, which is most often near a joint. The pain and tenderness are out of proportion to the clinical evidence and are due to extreme tension within an unyielding tissue. The roentgenographic findings in the early, acute stage of osteomyelitis are of no value in determining the diagnosis.

In the event there is a delayed diagnosis in the seriously ill patient, the end-results obtained in the treatment of osteomyelitis may be far from encouraging, and the mortality high. An early diagnosis is important in obtaining the best results. The diagnosis having been made after a careful study, the patient is prepared and operative treatment is instituted at the site of the diseased focus.

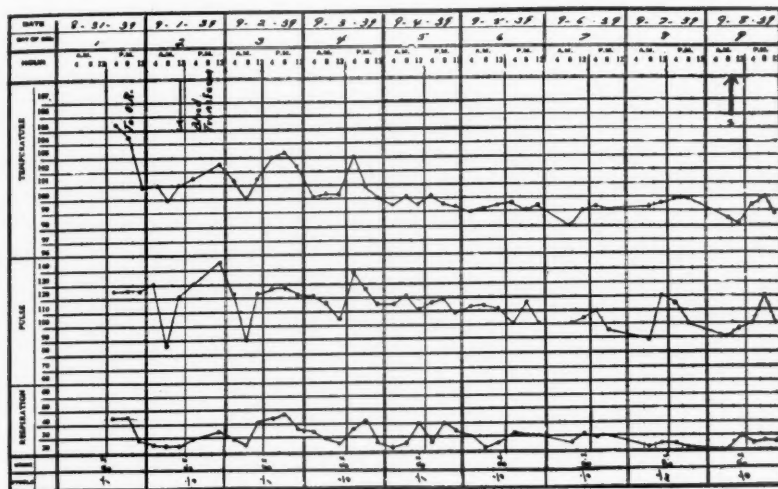


CHART 1.—Case 5: Showing the temperature curve.

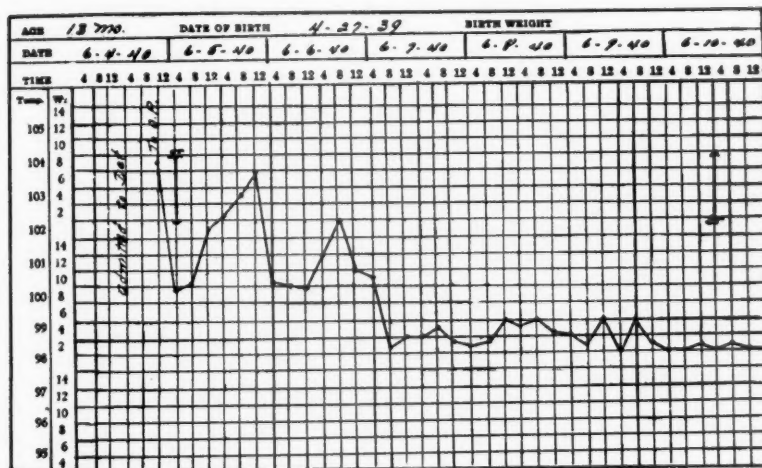


CHART 2.—Case 9: Showing the temperature curve.

The proper time for surgical drainage is a controversial question⁷ but, from our experience, early operative intervention combined with chemotherapy is the procedure of choice. Decompressing the shaft of the bone at the site of the lesion offers relief from pain and affords drainage, thereby minimizing the continuance of a septicemia from this focus.

The surgical procedure should be carried out with as little trauma as possible to the patient and with a minimum time for operating. The periosteum is treated gently and separated sufficiently to permit exposing the cortex over the cancellous bone which is drilled according to the usual technic. The cortex between the two or three drill-holes is removed to allow adequate drainage. Since the disease has existed for several days, the pus will usually be under such pressure as to exude around the drill before the latter is removed. The cavity is packed loosely with vaselined gauze¹⁵ and the extremity immobilized in a plaster dressing or mold. Intravenous saline and glucose solutions supplemented by small blood transfusions are given before and after operation as indicated. The surgical management of the suckling child is not as radical. The cortex of the bone in the infant is thin, and early perforation results with formation of a superficial abscess which can be drained. In the older child, the same conservative form of surgical procedure is practiced where the flat bones of the pelvis are involved; for instance, when the disease attacks the ilium, the cortex perforates early, forming a superficial abscess which may be drained. A resection of the diseased portion of the involved bone may be indicated by subsequent roentgenologic findings.

With the introduction of sulfanilamide therapy, the treatment of certain types of infection, particularly those due to the pneumococcus, meningococcus, gonococcus and certain forms of streptococci, immediately showed a high proportion of favorable results, as reported in a large number of published articles.^{9, 12, 5} However, favorable effects on infections resulting from staphylococci invasion were not apparent. Soon after the drug became available, we used it in a number of cases of acute osteomyelitis, most of which were of staphylococcal origin, and the results were discouraging. We were, therefore, forced to continue reliance on surgical drainage of local lesions, blood transfusions, and occasional antitoxin treatment for the relief of this serious disease. There was continued improvement in the mortality rate; however, many of the patients developed secondary lesions; there were many secondary operations, and often progressive bone destruction occurred, leading to long periods of morbidity and serious crippling deformities.

With some skepticism, we instituted sulfapyridine therapy, and the first patient was treated in February, 1939. Clinical investigation of this form of treatment as reported by Long,¹⁰ and others,^{11, 14} indicated a favorable effect on certain types of staphylococcal septicemia, and it seemed logical to assume that patients suffering from sepsis associated with bone infection might also be benefited (Charts 1 and 2). The results obtained with sulfapyridine therapy were encouraging from the onset and it was soon apparent that a valuable addition to the treatment of septicemia associated with staphylococcal osteomyelitis was available.

In February, 1940, sulfathiazole was supplied for experimental use in the treatment of infected bone lesions. Our results have not indicated that this preparation is more effective than sulfapyridine in the treatment of staphylococcal bone infections and the associated septicemia. The drug, however, has

been better tolerated by some of our patients, and for this reason has been substituted in practically all of our cases of this type since this therapeutic agent has been available. Practically all of the patients have tolerated sulfathiazole well and only in a few instances have gastric disturbances of any severity occurred. Dermatitis has been occasionally observed but has not been severe enough to necessitate discontinuance of the therapy. With the exception of an occasional mild hematuria, disturbances in renal function thus far has not been apparent. Acetylsulfathiazole crystals have been observed in the urine of a number of patients under treatment but have not given rise to symptoms. Cyanosis has seldom occurred and temperature reactions have not been considered a result of the administration of the drug.

Blood determination of hemoglobin, methemoglobin and sulphhemoglobin have been routinely made in conjunction with blood level estimations of the drug. These studies have not indicated serious changes even when fairly high blood levels have been maintained for a number of days. Oral administration of the drug has been possible in nearly all cases. In one patient, intravenous administration of the sodium salt of sulfathiazole was necessary because of continued vomiting after oral treatment, and the drug was well-tolerated. The dosage was calculated on the basis of the patient's weight. One and one-quarter grains per pound of weight was given over a 24-hour period, divided and administered at four- or five-hour intervals. We found that this amount was usually effective, and a blood level near 4 mg. per 100 cc. was maintained. In cases where the blood level fell below this point the clinical response was usually satisfactory, and rarely was the dosage increased. It has not been found necessary to give large doses at the onset of the treatment, but they are usually well-tolerated and may aid in a more rapid sterilization of the blood stream by inhibiting the growth of organisms. As the patient's temperature subsided and the general condition improved, the amount of the drug was gradually reduced. Administration of this preparation was continued for several days after the temperature approached a normal level and clinical improvement was apparent.

Only recently have we considered the use of a sulfonamide derivative as a part of the local treatment of chronic osteomyelitis. During the past few weeks, following sequestrectomy and saucerization, in a number of patients with chronic osteomyelitis, we have packed the cavities with sulfathiazole powder. Insufficient time has elapsed to permit an expression of opinion regarding the value of this method of therapy. We have not employed any of these drugs locally in the cavities produced surgically in the treatment of the acute stage of the disease, although, apparently, no contraindication to such treatment exists. According to a number of published reports,^{6, 8, 3} the local use of sulfanilamide in the treatment of compound fractures has either resulted in a marked decrease in the occurrence of complicating bone infections or has aided in combating such infections when present.

Articles reporting the results from the chemotherapy type of treatment, particularly in pneumonia, predominate in the medical literature.^{4, 16, 2} Scat-

tered reports have appeared during the past year citing favorable results from chemotherapy in osteomyelitis, but, to date, we have found no record of treatment in any large series of cases. Although the series, herewith reported, is not very large, we believe a résumé of our experience during the past 22 months in the treatment of this disease is justified by the results obtained.

CASE REPORTS

Case 1.—A. K., white, male, age 11, was admitted, February 4, 1939, complaining of pain in the left hip region of two weeks' duration. The symptoms followed a fall while tobogganing. Examination revealed an acutely ill, extremely toxic child with a rectal temperature of 103° F. There was swelling of the left hip region although the leg could be flexed at the hip joint without pain. There was great tenderness on pressure over the left ilium in the region of the anterior superior spine and considerable swelling along the iliac crest. W.B.C. 15,800, with 80 per cent polymorphonuclears. Roentgenologic examination revealed a limited demineralization in the region of the left iliac crest. A diagnosis of acute osteomyelitis of the left ilium was made.

At operation, an abscess was found located subperiosteally and extending laterally as well as mesially to the ilium in the region of the anterior superior spine. The bone was soft and spongy and exuding purulent material. Approximately one-third of the ilium was resected subperiosteally. A culture of the exudate from the abscess gave a growth of *Staphylococcus aureus*. The postoperative course was unsatisfactory. The patient remained toxic. Blood cultures were negative. Sulfanilamide was given and small transfusions administered. The temperature declined but the patient still remained listless and appeared toxic. The administration of sulfapyridine was started in doses of 12 gr. every four hours, four days after operation. The patient responded well, with a further drop in temperature to normal. He became alert and interested in his surroundings and the appetite became much improved. Swelling decreased and the amount of discharge was considerably diminished in one week. The sulfapyridine blood level was maintained between 4.8 and 8.5 mg. per 100 cc. for ten days, when the drug was discontinued. The patient's general condition continued to improve and he was discharged to the Convalescent Hospital in four weeks. Wound healing was complete in four months, and the patient was symptom-free.

Case 2.—N. P., white, female, age eight, was admitted to the Medical Service, February 11, 1939, complaining of pain in the region of the right knee of six days' duration. Examination revealed a moderately ill child, with a rectal temperature of 102° F. There was considerable tenderness and swelling just below the right knee and a possible diagnosis of osteomyelitis was considered. Hot compresses were applied and sulfapyridine administration begun in a dose of 7.5 gr. every four hours. W.B.C. 14,250, with 82 per cent polymorphonuclears. On February 15, 1939, the patient was referred to surgery. At this time, a soft tissue abscess was found below the right knee and operation was advised.

Incision down to the tibia was carried out and a trephine of the bone performed. The cortex was soft and a small amount of purulent material exuded from the drill-holes. A blood culture, taken on admission, gave a growth of *Staphylococcus aureus*; cultures of the exudate from the abscess of the leg showed the same organism. The child's temperature declined to normal in two days and the general condition improved. Sulfapyridine was discontinued on the sixth day following operation. The wound continued to discharge but in gradually decreasing amounts, while the child's general condition rapidly improved. She was discharged home on the twenty-third postoperative day. Further progress in the healing was noted on the return visits to the Out-Patient Department. A small sequestrum was expelled about six weeks following discharge, after which the wound healed rapidly. There was complete closure in five months, and the patient was walking without discomfort.

Case 3.—A. P., white, female, age 11, was admitted to the Medical Service, July 6, 1939, with a two-day history of pain and swelling of the right ankle, accompanied by a high fever. A tentative diagnosis of rheumatic fever was made. This child had a long previous history of pyuria with treatment in the genito-urinary clinic for over three years before this admission. Examination revealed an acutely ill child with a rectal temperature of 103° F., and swelling about the right ankle. W.B.C. 11,500. The patient was referred to surgery eight hours after admission. The temperature at that time was 105° F., and the child had considerable pain. A diagnosis of acute osteomyelitis of the lower right tibia was made, and immediate incision and drainage was carried out, with the liberation of a large collection of pus beneath the periosteum.

The operation included a trephine of the bone and liberation of purulent exudate from the cancellous area just above the epiphysis. The administration of sulfapyridine gr. 10, every four hours, was begun. There was a rapid decline in the temperature to normal in four days and the patient was sitting up and enjoying a regular diet at that time. The general condition was such that she was discharged to her home on the eighth postoperative day. A blood culture, taken on the date of admission, was reported positive for *Staphylococcus aureus* and the culture of the exudate from the operative site showed a growth of hemolytic *Staphylococcus aureus*. A blood level of sulfapyridine on the second postoperative day was 6.6 mg. per 100 cc. and the drug was discontinued two days later. The subsequent course has shown slow healing of the lesion. A sequestrectomy was performed six months following the initial operation and a saucerization 11 months from the date of the first operative procedure. The wound continued to heal slowly, but was completely closed three months following the last operation. Roentgenograms show satisfactory bone regeneration.

Case 4.—W. A., white, male, age four, was admitted, July 6, 1939, with a history of sore throat and fever one month previously. Two weeks before admission the child began to complain at night of pain just below the right knee. Swelling and tenderness of this area appeared, accompanied by a high fever. A superficial abscess of the upper right leg was incised by a physician the day before admission. The rectal temperature on entering the hospital was 101° F., and the child, though pale, weak and evidently undernourished, did not appear acutely ill. Roentgenologic examination revealed irregularity of the bone structure at the proximal end of the right tibial diaphysis. In view of the probable inadequate drainage, a further operative procedure was carried out the day following admission.

A large soft tissue abscess was opened widely and a window cut in the cortex of the upper tibia. The bone was found soft and necrotic. The wound was packed with vaselined gauze and the extremity immobilized in plaster. As a precautionary measure, sulfapyridine in doses of 7.5 gr., every five hours, was administered. Convalescence was uneventful and the child was discharged on the thirteenth day after admission. The subsequent course showed complete healing of the lesion without sequestration in four months, and there has been no reactivation of the infectious process.

Case 5.—M. C., white, male, age seven, was admitted, August 31, 1939, with a history of one week's duration of symptoms, including pain and swelling of the right leg. On the third day of illness, the patient was placed in a contagious hospital with a diagnosis of anterior poliomyelitis. After four days, the diagnosis of acute osteomyelitis was made and the patient was transferred to the Children's Hospital. Examination revealed a critically ill child, with a rectal temperature of 105° F. He was unconscious and practically in a moribund condition, with a barely perceptible pulse. The upper left leg was markedly swollen and discolored, and fluctuation was present. W.B.C. 6,700, with 84 per cent polymorphonuclears.

After preparation with intravenous fluids and, as a rather desperate measure, a rapid incision and drainage of the upper right tibia was carried out. A large subperiosteal abscess was drained and a window cut in the cortex of the bone. The wound was packed open with vaselined gauze and a posterior plaster mold applied. Following operation, intravenous fluids and a blood transfusion were administered. In a few hours the oral

administration of sulfapyridine gr. 15, every six hours, was begun and well-tolerated. The blood cultures on admission gave a growth of *Staphylococcus aureus*, with hemolytic *Staphylococcus aureus* recovered from the lesion of the tibia. The patient's condition following operation rapidly improved, with the temperature reaching normal on the fifth day. On the third postoperative day, the patient sat up in bed, played games and took a liberal diet. Sulfapyridine was discontinued on the eighth day following operation. The patient was discharged to the Convalescent Hospital on the eighteenth postoperative day. The subsequent course was uneventful and without further interference. The patient was sent home two months later with the wound practically healed. A month after discharge the wound was entirely healed and the patient was walking on crutches. Serial roentgenograms have shown progressive healing without evidence of sequestrum formation. When last seen, in August, 1940, there were no complaints, and the patient was walking normally.

Case 6.—H. R., white, female, age two and one-half, was admitted, August 31, 1939, from the City Contagious Hospital, where she had entered the day before with a tentative diagnosis of anterior poliomyelitis. There was a history of a limp affecting the right leg following a fall one week previously. Examination revealed a critically ill child with swelling about the right hip region and pain with motion of the joint. The rectal temperature was 105° F. W.B.C. 10,500, with 68 per cent polymorphonuclears. Aspiration of the hip joint revealed the presence of thick green pus.

After preparation with intravenous saline and glucose solution, the hip joint was entered through a posterior incision. A large amount of purulent material was evacuated. Rubber tissue drains were inserted into the joint cavity and the wound packed with vaselined gauze. A plaster hip spica was applied. A blood culture on admission and exudate from the hip joint gave a growth of *Staphylococcus aureus*. As soon after operation as possible the patient was given sulfapyridine gr. 3.75, every four hours. This was continued for 19 days, and the blood level maintained at 3.5 to 3.7 mg. per 100 cc. Four small blood transfusions were administered over a period of three weeks. The patient's general condition rapidly improved, and the temperature gradually declined to normal in the course of five days. There was a moderate amount of purulent discharge from the operative wound, gradually decreasing and, on the thirty-sixth postoperative day, the patient was discharged to the Convalescent Hospital. Due to poor home conditions the patient has been kept at the hospital, although the wound has been healed for several months and roentgenograms show advanced healing of the lesion of the neck of the femur.

Case 7.—A. P., white, girl, age four, was admitted, January 29, 1940, with a history of pain and swelling about the right knee over a three-day period. Examination revealed an acutely ill child with a rectal temperature of 103° F., and pain and swelling in the region of the right knee joint and the lower third of the right thigh. W.B.C. 15,800, with 86 per cent polymorphonuclears. The right knee joint was aspirated shortly after admission and a few cubic centimeters of cloudy fluid obtained. This fluid gave a positive culture of *Staphylococcus aureus*. A blood culture taken on admission showed hemolytic *Staphylococcus aureus*.

After preparation with intravenous fluids a large subperiosteal abscess of the lower right femur was drained. A fenestra was placed in the cancellous bone just above the epiphyseal cartilage. The wound was packed open and immobilized with a heavy posterior plaster mold. Purulent exudate from the abscess yielded a growth of *Staphylococcus aureus*. A few hours after operation, sulfapyridine was given orally in doses of gr. 7.5, five times daily. The blood level was maintained from 5 to 6.5 mg. per 100 cc. for nine days. The patient's condition appeared satisfactory and the temperature was normal on the seventh day after operation. At the request of the clinical bacteriologist of the hospital, sulfathiazole was substituted for the sulfapyridine on the ninth day and given in doses of 7.5 gr., five times daily. The temperature rose to 103° F. rectally two days later, then declined and remained normal. The patient was discharged to the Convalescent Hospital on the twenty-third day following operation, with the extremity immobilized in a plaster spica dressing. The general condition has remained excellent and bone regenera-

tion has been gradual. There has been no evidence of sequestrum formation. Recent roentgenograms showed narrowing of the joint space of the right knee and demineralization of the bone structure about the joint. At present, November 11, 1940, there is an intermittent discharge of small amounts of purulent material from the operative wound.

Case 8.—L. A., white, female, age six, was admitted, April 20, 1940, with a history of pain and swelling of the left leg, persisting over a period of two weeks. Examination revealed an acutely ill child with a rectal temperature of 103° F. The upper one-half of the left leg was greatly swollen and markedly tender. Fluctuation was present. Roentgenologic examination revealed characteristic signs of an acute osteomyelitis of the upper left tibia. W.E.C. 27,600, with 68 per cent polymorphonuclears. A blood culture taken on admission gave a growth of *Staphylococcus aureus*.

The operative procedure consisted of drainage of a large soft tissue abscess and a trephine of the shaft of the tibia. A fairly large fenestra was cut in the cortex and considerable thick purulent material was evacuated from the medullary canal. The wound was packed open and a heavy posterior plaster mold applied. Cultures of the exudate from the abscess gave a growth of *Staphylococcus aureus*. Within a few hours after operation, the patient was able to take sulfathiazole in doses of 12 gr., every four hours. A blood transfusion was given the following day. The temperature subsided promptly to normal on the third day following operation, and remained normal until discharge to the Convalescent Hospital on the eleventh postoperative day. A blood culture on the eighth postoperative day gave no growth. Sulfathiazole was discontinued on the ninth day after operation. A blood level of 3.2 to 4.3 mg. per 100 cc. was maintained throughout administration.

Subsequent progress was satisfactory, with rapid subsidence of discharge and marked improvement of the patient's general condition. Roentgenologic examination two months after operation revealed a number of small sequestra, and these were removed June 22, 1940, without any attempt at extensive saucerization. The wound healed completely within eight weeks, and the patient was allowed to walk on crutches. On examination, November 1, 1940, there were no symptoms and no signs of reactivation of the inflammatory process.

Case 9.—O. R., white, male, age 13 months, was admitted, June 4, 1940, with a history of refusal to use the right leg for two and one-half weeks. Swelling in the right hip region accompanied by a high fever had been present for a three-day period before admission. The patient was treated at the hospital two months previously for bronchopneumonia. Examination revealed an acutely ill child, with a rectal temperature of 104° F. The right hip was held flexed and externally rotated. There was considerable swelling about the hip region, and pain with attempted movement. Roentgenologic examination confirmed the diagnosis of an osteomyelitis of the neck of the right femur, and subluxation and lateral displacement of the femoral head was noted. W.B.C. 24,800, with 78 per cent polymorphonuclears. Unfortunately a blood culture was not taken.

A few hours after admission, and following preparation with intravenous fluids, drainage of a large submuscular abscess posterior to the right greater trochanter was carried out, together with incision of the hip joint and evacuation of a considerable amount of purulent material. A culture of the pus from the joint gave a growth of hemolytic streptococci. The wound was packed and a plaster hip spica applied. Sulfathiazole in doses of 7.5 gr., every eight hours, was given orally following reaction from the anesthetic, and was well-tolerated. The dosage was changed to gr. 3.75, every four hours, the following day. The sulfathiazole blood level was 8.8 mg. per 100 cc. after the administration of several doses but fell to 1.4 mg. two days later. The temperature dropped rapidly to normal within 50 hours and remained at this level. Sulfathiazole was discontinued on the sixth postoperative day. The amount of discharge from the incision decreased gradually. The patient was discharged to the Convalescent Hospital on the tenth postoperative day. Healing of the lesion in the femur has progressed gradually, and the general condition has been satisfactory. Roentgenologic examination, October 2, 1940,

showed resolution of the inflammatory process and a decrease in the lateral displacement of the femoral head.

Case 10.—E. F., white, female, age six, was admitted, June 4, 1940, with a history of pain and swelling of the lower left leg of 24 hours' duration. The symptoms occurred a few hours after a fall from a swing. Examination revealed an acutely ill girl with a rectal temperature of 105° F. The lower left leg was swollen and very tender over the lower one-third of the crest of the tibia. W.B.C. 9,200, with 64 per cent polymorphonuclears.

Intravenous fluids were administered, following which incision and drainage was carried out and a fenestra placed in the cortex of the lower left tibia. No frank pus was encountered at any point but there was considerable edema of the soft tissues. The wound was packed and partially closed by sutures. A posterior plaster mold was applied. A culture of material from the cancellous bone gave no growth while a culture of fluid from the soft tissues gave a growth of *Staphylococcus aureus*. No blood cultures were taken. Although the findings at operation were not significant of a clinical osteomyelitis, the extreme bone tenderness, together with roentgenologic findings five days after operation indicating a pyrogenic inflammatory process, appeared to justify a diagnosis of early osteomyelitis. The patient was given 30 gr. of sulfapyridine as soon as she reacted, and this was followed by doses of 15 gr., every six hours. She was given a blood transfusion on the second postoperative day. The temperature dropped rapidly to normal on the second day following operation, and was maintained at this level until discharge from the hospital. Sulfapyridine was discontinued on the third postoperative day because of the patient's rapid improvement. She was discharged on the twelfth postoperative day. The wound discharged very small amounts of seropurulent material, and healed entirely in six weeks. The patient discontinued the use of crutches, August 30, 1940, 12 weeks following operation. When seen, October 18, 1940, there were no symptoms, and the patient was walking normally.

Case 11.—P. G., white, male, age four, was admitted to the hospital, February 22, 1940, with a history of upper respiratory infection two weeks previously. Six days before admission he complained of a sore throat, fever and pain in the left knee. Examination showed an acutely ill child with a rectal temperature of 101° F. The left knee was swollen and there was evidence of an effusion in the joint. W.B.C. 19,400, with 82 per cent polymorphonuclears. Blood culture, February 22, showed *Streptococcus haemolyticus*. Sulfanilamide gr. 30 was given on day of admission, and gr. 7.5, every six hours, thereafter. Blood level was 4.5–11.4 mg. Aspiration of the left knee joint, February 27, revealed cloudy fluid, which on culture showed *Streptococcus haemolyticus*. The temperature remained normal but there was a localized area of tenderness over the lower third of the femur. On March 5, 1940, a trephine of the cancellous portion of the femur was performed; a small amount of pus being obtained. The cortex was removed between the drill-holes, and the wound packed lightly with vaselined gauze. A posterior mold was applied. The pus on culture revealed *Streptococcus haemolyticus*. Sulfanilamide was continued postoperatively, and the level maintained at 10.6–11.8 mg.; it was discontinued entirely March 17. His convalescence was rapid and he was discharged from the hospital March 23. The wound was completely healed one month after discharge and follow-up, six months later, revealed child had complete range of motion of the knee joint.

Case 12.—M. B., white, female, age 13, was admitted to the hospital, November 4, 1940, with a history of severe pain in the left leg of six days' duration. Examination revealed an acutely ill child, with a rectal temperature of 101° F. There was exquisite tenderness over the upper third of the left tibia. W.B.C. 15,450, with 82 per cent polymorphonuclears. A diagnosis of acute osteomyelitis was made, and four hours after admission temperature was 104° F.

An immediate incision and drilling of the left tibia with removal of the cortex between the drill-holes was carried out just below the epiphysis, and free pus escaped along the drill. The wound was lightly packed with vaselined gauze and the leg immobil-

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ized in a posterior plaster mold. Sulfathiazole, gr. 30 was given every four hours, beginning the first postoperative day. The blood sulfathiazole level, November 7, was 3.1 mg. The temperature gradually approached normal and remained entirely normal after November 13. Three transfusions of 250 cc. were given during the postoperative period. Culture of the pus from the tibia revealed *Staphylococcus aureus haemolyticus*. Drainage from the wound was quite profuse for the first week postoperatively but gradually dimin-

TABLE I
A Study from February, 1939 to December 1, 1940.

ACUTE OSTEOMYELITIS TREATED OPERATIVELY AND WITH SULFONAMIDE COMPOUNDS

CASE	SEX	AGE	ILLNESS BEFORE ADMIT.	TEMP.	FOCUS	OPERATION	BACTERIOLOGY		HOSP.	THERAPEUTICS	END RESULT
							WOUND CULTURE	BLOOD CULTURE			
A.K.	M.	11	14 DA	103°	LF. ILEUM	YES. RESECTION OF PORTION	STAPH. AUREUS	—	28 DA	SULFANILAMIDE 4 DAYS SULFAPYRIDINE 10 DAYS	GOOD
H.P.	F.	8	6 DA	102°	RT. TIBIA	YES. FENESTRA	STAPH. AUREUS	+	23 DA	SULFAPYRIDINE 8 DAYS AFTER OPERATION	GOOD SMALL SEQUESTRUM DISCHARGE
A.P.	F.	11	3 DA	105°	RT. TIBIA LOWER	YES. FENESTRA	STAPH. AUREUS HEMOLYTICUS	+	8 DA	SULFAPYRIDINE 8 DAYS	GOOD SAUCERIZATION 11 MONTHS
W.A.	M.	4	14 DA	101°	RT. TIBIA	YES. FENESTRA AND DRA. OF ABSCESS	NO RECORD	NO RECORD	13 DA	SULFAPYRIDINE 5 DAYS	GOOD 4 MONTHS
M.C.	M.	7	7 DA	105°	RT. TIBIA	YES. FENESTRA	STAPH. AUREUS HEMOLYTICUS	+	18 DA	SULFAPYRIDINE 8 DAYS	GOOD
H.R.	F.	2½	7 DA	105°	RT. FEMUR NECK	YES. DRAINAGE OF JOINT	STAPH. AUREUS	+	36 DA	SULFAPYRIDINE 19 DAYS	LESION TREATED 1 YR.
A.P.	F.	4	3 DA	103°	RT. FEMUR LOWER	YES. FENESTRA	STAPH. AUREUS	+	23 DA	SULFAPYRIDINE 9 DAYS SULFATHIAZOLE 11 DAYS	STILL SOME DISCHARGE NO SEQUESTRUM
L.A.	F.	6	14 DA	103°	LF. TIBIA UPPER	YES. FENESTRA	STAPH. AUREUS	+	11 DA	SULFATHIAZOLE 9 DAYS	SEQUESTRECTOMY 2 MONTHS WOUND HEALED IN 8 WEEKS
G.R.	M.	13MO	18 DA	104°	RT. FEMUR NECK	YES. DRAINAGE OF HIP-JOINT	STREP. HEMOLYTICUS	NO RECORD	10 DA	SULFATHIAZOLE 6 DAYS	WOUND HEALED SLIGHT DISLOCATION IMPROVED
E.P.	F.	6	1 DA	105°	LF. TIBIA LOWER	YES. FENESTRA	STAPH. AUREUS SOFT TISSUE	NO RECORD	12 DA	SULFAPYRIDINE 3 DAYS	HEALED IN 6 WEEKS
P.G.	M.	4	14 DA	101°	LF. FEMUR LOWER	YES. FENESTRA	STREP. HEMOLYTICUS	STREP. HEM. ON ADMISSION	30 DA	SULFANILAMIDE 18 DAYS BEFORE AND AFTER OPER.	LITTLE DRAINAGE SUPPURATIVE KNEE- JOINT SUBSIDED
M.B.	F.	13	6 DA	102°	LF. TIBIA UPPER	YES. FENESTRA	STAPH. AUREUS HEMOLYTICUS	—	16 DA	SULFATHIAZOLE 9 DAYS AFTER OPERATION	GOOD LITTLE DISCHARGE
G.W.	M.	6	11 DA	102°	RT. FEMUR LOWER	YES. FENESTRA	STREP. HEM. ALSO IN KNEE-JOINT	—	35 DA	SULFATHIAZOLE 13 DAYS	GOOD FOR OSTEO LIMITATION OF MOVEMENT IN KNEE-JOINT.
G.K.	M.	2½	2 DA	104°	LF. FEMUR LOWER	YES TREPINE	STREP. HEM. ALSO IN KNEE-JOINT	NO RECORD	12 DA	SULFATHIAZOLE 12 DAYS	IMPROVED STILL IN HOSPITAL

ished, and the patient was allowed up in a wheel chair, November 12, and discharged from the hospital November 20.

Case 13.—G. H., white, male, age six and one-half, was admitted to the hospital, April 28, 1940, with a history of pain and swelling in the right knee and thigh for 11 days. The latter symptoms followed an upper respiratory infection of three days' duration. Examination revealed an acutely ill child, with tenderness over the lower third of the right femur, and evidence of fluid in the right knee joint. Rectal temperature was 102.4° F. W.B.C. 20,800, with 90 per cent polymorphonuclears.

Four hours after admission, under general anesthesia, the right knee joint was aspirated and cloudy fluid obtained. An incision was then made over the lateral aspect of the right femur, drill-holes were made in the cancellous portion, and some thin pus obtained. The cortex between the drill-holes was removed and the wound packed lightly with vaselined gauze. The leg was immobilized in plaster. Cultures from the right femur

and knee joint revealed *Streptococcus haemolyticus*. A blood transfusion was given, April 30, and the temperature ranged from 101° to 103° F. Sulfathiazole gr. 15 was given, May 1, and repeated every four hours; the blood level, May 4, was 4.0 mg. The general postoperative course was smooth except for occasional temperature rise to 100° F. He was discharged from the hospital June 2. He was readmitted, June 19, because of swelling and pain in the right knee joint and the traction applied in extension. On June 21, aspiration of fluid from the right knee joint was attempted but none was obtained. The wound in the thigh was healed June 12. Local heat and traction were continued and the patient was discharged home, June 26, with a brace. He was readmitted, September 28, and, under general anesthesia, manipulation revealed full extension and 90° flexion. He was last seen on November 25, at which time there was evidence of thickening of the joint capsule, complete extension but flexion limited to 20°.

Case 14.—G. K., white, male, age two and one-half, was admitted to the Medical Service, November 21, 1940, with a history of pain in the left knee of two days' duration. A high fever had been present since the onset of the illness, and swelling of the knee had developed several hours before entering the hospital. Examination revealed an acutely ill child with a rectal temperature of 103.8° F. The left knee was moderately swollen and very tender to palpation. The joint could be moved through a range of 45° without pain. W.B.C. 23,600, with 72 per cent polymorphonuclears. The patient was referred to the Surgical Service, November 23. At this time, the swelling of the knee was still present and, in addition, there was localized tenderness and moderate swelling over the lower one-third of the left femur. Immediate operation was advised.

The knee joint was aspirated and 4 cm. of thin cloudy fluid obtained. A lateral incision was made over the lower left femur. The periosteum was incised, and drill-holes placed through the cortex. A small amount of cloudy fluid exuded from the lower drill-openings. The wound was partially closed after packing with vaselined gauze, and a posterior plaster mold applied. Cultures of the fluid from the knee and from the drill-holes in the femur both gave a growth of *Streptococcus haemolyticus*. Sulfathiazole gr. 15 was given shortly after admission, continued in doses of 7.5 gr., every four hours, and was well-tolerated. The temperature declined to normal in 48 hours, and has remained at that level. The patient's general condition has greatly improved and there has been no complaint of pain since operation. On December 2, 1940, the patient was sitting up in bed and taking a regular diet. There was a moderate amount of seropurulent drainage from the wound. The sulfathiazole was discontinued on the twelfth day following admission.

The following cases are considered as a separate group because of a question in diagnosis; because of the presence of a complicating condition; or because of a change from the usual routine of treatment. These histories are not complete but are included because they represent added experience with chemotherapy in a varied number of bone and joint lesions.

Case 15.—E. W., male, age nine, was admitted, May 13, 1940, with a history of pain in the upper right arm of one week's duration. Examination revealed an acutely ill child with a rectal temperature of 103° F. The right shoulder was markedly swollen and painful to palpation.

Incision and drainage of the right shoulder joint was carried out shortly after admission, and a large amount of pus evacuated. Purulent exudate was found subperiosteally in the upper humerus, and drill-holes were placed into the cancellous portion of the bone. No pus was noted after trephining. The arm was immobilized in a plaster shoulder spica, in a position of abduction. Sulfathiazole was given in doses of 30 gr., four hours apart, for a total of 60 gr., and then administered in doses of 15 gr., five times daily. Intravenous fluids and a blood transfusion were given. Convalescence was uneventful. The temperature reached normal in 48 hours, and the patient's general condition improved rapidly.

Sulfathiazole was discontinued on the eighth postoperative day, and the patient was discharged on the thirteenth day after operation. The wound was completely healed in four weeks. On examination, three months after operation, there was a complete range of motion in the shoulder joint.

Case 16.—D. C., white, female, age six, was admitted to the Medical Service, March 27, 1939, with a diagnosis of acute rheumatic fever. Localizing symptoms developed in the right hip region several days later and the patient was transferred to the Surgical Service. A blood culture was positive for *Streptococcus haemolyticus*. Treatment consisted of immobilization with plaster, and sulfanilamide in doses of 10 gr., every six hours, over a period of 37 days. A soft tissue abscess developed in the right groin and was drained. A number of blood transfusions were administered. Roentgenologic studies showed progressive destruction of the head and neck of the right femur and the acetabulum. Soon after admission a serious cardiac lesion developed. Recovery has been slow, and the patient has been continuously immobilized during the interval of 19 months since admission in plaster spica dressings. There is considerable discharge from the sinus in the right groin at present. Recent roentgenologic studies showed some healing of the bone lesion, and evidence of beginning ankylosis. The patient's general condition is improved although there has been little change noted on repeated examinations of the heart.

Case 17.—B. R., white, female, age three, was admitted, September 10, 1940. The patient had been operated upon elsewhere, one year previously, and a soft tissue abscess of the upper right leg was drained. The wound has drained intermittently since. The day before admission, the leg became swollen and tender and the patient had chills and fever. On examination, there was considerable swelling and tenderness over the lateral aspect of the upper right leg. Roentgenologic study showed an extensive osteomyelitic process of the upper portion of the shaft of the right fibula.

At operation, the upper fibula was found necrotic and a considerable portion of the shaft was excised subperiosteally. The wound was partially closed and then packed with vaselined gauze. A posterior plaster mold was applied. Sulfathiazole was given in doses of 12 gr., every five hours. The child's general condition rapidly improved. The rectal temperature dropped from 103° F. on admission, to normal in 24 hours, and remained at that level. The patient was discharged on the twelfth postoperative day, with the wound discharging a small amount of purulent material. On November 1, 1940, the wound was nearly healed. The patient's general condition was excellent, and roentgenograms showed evidences of healing.

Case 18.—L. B., white, male, age four, was admitted, August 18, 1940 with a history of pain and swelling of the upper left leg over a period of four weeks. The patient had a cold just prior to the onset of pain in the leg. The child was treated by three physicians in turn and finally sent to the hospital. One physician had incised a soft tissue abscess of the upper right leg. Examination revealed swelling and tenderness of the upper one-half of the left leg. The temperature was normal. Roentgenograms showed a diffuse destructive process of the tibial diaphysis characteristic of osteomyelitis. With bed-rest the pain and tenderness subsided and the child was transferred to the Convalescent Hospital six days after admission. He was readmitted seven days later acutely ill, with a recurrence of pain and tenderness in the left leg and a rectal temperature of 104° F. A blood culture was positive for *Staphylococcus albus*. Hot compresses were applied to the leg, and sulfathiazole administered in doses of 7.5 gr., every four hours. The temperature subsided to normal in 24 hours, and the local symptoms in the leg rapidly disappeared. The temperature remained normal and the general condition of the patient was much improved. The child was discharged on the fourteenth day after admission. Since discharge, the patient has been observed at weekly intervals. The leg remains somewhat swollen but not tender. Roentgenograms show extensive periosteal proliferation and development of a large sequestrum. Operative measures, to include sequestrectomy and saucerization, will be carried out at an early date.

Case 19.—J. S., white, male, age nine, was admitted to the Medical Service, June 27, 1940, with a history of pain in the region of the left knee for a period of three days. Examination revealed an acutely ill child, with a rectal temperature of 104° F. The left knee was swollen and there was pain on pressure over the lower left femur. The blood



FIG. 1.—Case 2: Radiograms of N. P. (A) March 8, 1939. (B) February 19, 1940.



FIG. 2.—Case 5: Radiograms of M. C. (A) October 27, 1939. (B) January 12, 1940.

culture was positive for *Staphylococcus aureus*. After consultation, the patient was transferred to the Surgical Service and operation performed.

The knee joint was aspirated and a small amount of cloudy fluid obtained. The lower left femur was then drilled and pus escaped from the lower openings. A culture of the fluid from the knee, and pus from the femur, gave a growth of *Staphylococcus aureus*. Sulfathiazole gr. 15, five times daily, was administered, and continued in gradually decreas-

CHEMOTHERAPY IN OSTEOMYELITIS

ing doses for 21 days. The temperature fell rather slowly to normal; however, the patient's general condition rapidly improved. The swelling of the knee subsided in a few days, while at no time was there more than a small amount of discharge from the incision of the lower thigh. The patient was discharged on the twenty-third postoperative day. Some swelling of the knee has recurred since discharge and there is some limitation of motion. The surgical wound is healed. Roentgenograms show normal articular cartilage spacings of the knee joint, and some demineralization of the lower femur. There are no



FIG. 3.—Case 5: End-result in M. C. (ref. Fig. 2A and B), November 22, 1940. FIG. 4.—Case 1: End-result in A. K., December 27, 1939.

definite areas of bone destruction. On November 1, 1940, the child was walking on crutches and receiving physiotherapy treatments. His general condition was satisfactory.

The foregoing discussion and the case reports emphasize the value of chemotherapy in the management of acute osteomyelitis. The histories indicate that a number of the patients were treated before operation by some form of chemotherapy. The clinical picture of sepsis complicating osteomyelitis may be masked by previous chemotherapy, but local pain and tenderness persist. The early administration of sulfapyridine or sulfathiazole apparently controls the bacteremia and no doubt plays a prominent rôle in the prevention of secondary metastatic foci in other bones. In this series, treated by chemotherapy, none of the patients developed evidence of other bone involvement (Fig. 1, A and B—Fig. 2, A and B). It will also be noted that only two of the cases showed evidence of later sequestration.

It is interesting to note that Brown,¹ in 1939, reported the mortality of 160 cases of acute osteomyelitis, studied in seven hospitals, and found a 11.1 per cent mortality when surgery was delayed. Practically all of the cases in our series fall in the group classified as having had delayed operation. Brown further reports that operations performed when a blood stream infection was present, resulted in a 52.6 per cent mortality. He also found that 21.9 per cent of the patients having delayed operation showed secondary bone infection (Fig. 3 and Fig. 4).

It is apparent from our study that chemotherapy combined with early surgery, even in the presence of a blood stream infection, reduces mortality and lowers the incidence of secondary bone involvement (Table II and Fig. 5).

TABLE II
ACUTE OSTEOMYELITIS

YEAR	NO. OF PATIENTS	EXPIRED	MORTALITY RATE
1934	23	5	21.7%
1935	29	7	24.1%
1936	15	3	20.0%
1937	32	3	9.3%
1938	22	1	4.5%
1939	12	0	0.0%
JAN. 1 TO DEC. 1, 1940	7	0	0.0%
TOTAL	140	19	13.5%

CONCLUSIONS

Our experience with chemotherapy in this series of 19 patients treated for acute osteomyelitis leads us to the following conclusions:

(1) Osteomyelitis is one of the serious diseases of childhood.

(2) The mortality from septicemia associated with bone infections can be considerably reduced by sulfapyridine or sulfathiazole therapy, employed in conjunction with relatively early and adequate surgical drainage of the local lesion.

(3) The use of these drugs aids in limiting the amount of bone destruction and deformity, helps, apparently, in the prevention of secondary metastatic lesions, and favorably influences all types of complications in number and severity.

STUDY OF 140 PATIENTS WITH ACUTE OSTEOMYELITIS 1934-40

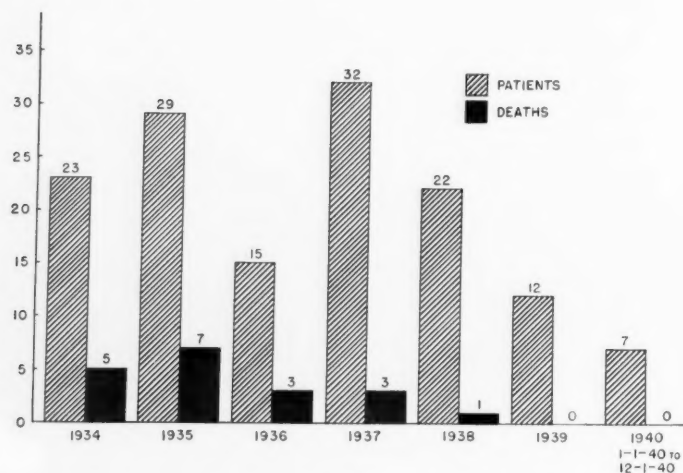


FIG. 5.

(4) Bone regeneration progresses more rapidly where this type of therapy is utilized, and ultimate healing occurs at an earlier date, thereby materially shortening the convalescent period.

Appreciation is expressed to Clifford D. Benson, M.D., for assisting in collecting some of the data.

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DISCUSSION.—DR. FRANK DICKSON (Kansas City, Mo.): Fracture of the neck of the femur has been described as the unsolved fracture, and it might, with equal truth, be said that hemorrhagic osteomyelitis might be described as the unsolved disease of bone. In the future, however, through the use of chemotherapy, it seems probable that we are going to have a different picture. Doctor Penberthy has presented a series of cases in which chemotherapy has been employed, in which the results have been most satisfactory. I thoroughly agree with him in his position of advocating immediate drainage of an acute osteomyelitic focus. I do not believe in postponing drainage indefinitely or

not operating at all. Naturally, one does not operate upon a dehydrated child, but it does not take long, with proper treatment, to get a patient into satisfactory condition, and then drainage, in our opinion, should be instituted at once. The shortening of the healing period and the excellent results presented by Doctor Penberthy, in his series, makes it one of the best end-result reports in the treatment of osteomyelitis with which I am familiar.

We have had some tremendously interesting experiences with osteomyelitis, acute and chronic, using chemotherapy in the last few months. We have used sulfathiazole exclusively. Instead of packing the wound with vaselined gauze after drainage, we have placed sulfathiazole crystals in the wound and closed it up tight. All have healed by primary union—not one has broken down! We have given sulfathiazole by mouth, when possible, before operation, and for as long as 18 days following operation, as well as introducing it into the wound. The results have been primary healing, and no mortality. If the results of the use of chemotherapy continue as promising as they are at the present time, I believe that we may look upon it as a boon in the treatment of this disease which, as Doctor Penberthy says, has, heretofore, left behind it a trail of more or less incapacitated and crippled individuals.

This paper was read before the Fifty-third Annual Session of the Southern Surgical Association, Hot Springs, Va., December 10, 1940.

BRIEF COMMUNICATIONS AND CASE REPORTS

DUODENAL RUPTURE AND FAT NECROSIS

REPORT OF TWO CASES

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DUODENAL RUPTURE, uncomplicated by gross injury to other abdominal organs, is rare, as is also pancreatic rupture. The two cases herewith reported concern duodenal rupture with fat necrosis but without evident pancreatic injury.

CASE REPORTS

Case 1.—A male, age 57, was admitted to the Surgical Service, Kings County Hospital, at 2 P.M., October 23, 1936, with a history of having been severely squeezed between two trucks, at the level of the lower anterior thorax and upper abdomen, at 7 A.M. of that day. He was unconscious for about an hour, then vomited—no blood.

Temperature 100° F., pulse 80, blood pressure 110/70. No evidence of peritonitis at that time. Observation was decided upon. There were 200 R.B.C. to the low power field found in the urine, and contusion of the kidney was diagnosed. The following day the temperature was unchanged; pulse had risen to 100; blood pressure 110/90. The patient was apprehensive. There was increasing abdominal rigidity, nausea but no vomiting. A plain roentgenogram of the abdomen was negative for air under the diaphragm. Perforated bowel was diagnosed and patient was operated upon.

Operative Pathology.—A large amount of beef broth-like peritoneal fluid was present, and fat necrosis was noted in the upper right quadrant. The pancreas was exposed through the gastrocolic omentum and found grossly normal; nothing was found in the lesser sac. There were several contusions of the jejunum and a moderate amount of retroperitoneal hemorrhage in the right lumbar gutter. A perforation, the size of a pea, was found in the anterior wall of the third portion of the duodenum through which duodenal contents was escaping. There was no induration surrounding the perforation to indicate an old process. The area surrounding the perforation was inflamed and covered with an exudate of lymph. The perforation in the duodenum was closed with two layers of sutures. The patient became uncontrollable and eviscerated during the third day. The abdomen was resutured at once with silver wire, but he died of bronchopneumonia six days after the first operation. No autopsy was obtained. There was, however, no evidence of continuing fat necrosis at the time of the second wound closure.

Case 2.—A male, age 46, was admitted to the Neurologic Service, Kings County Hospital, at 3.20 P.M., September 8, 1938, with a history of ten minutes' unconsciousness following an automobile accident. The patient was transferred to the Surgical Service after a skull fracture had been excluded. The significant findings were a small, deep laceration and contiguous brush-burn in the left upper abdominal quadrant, contusion and laceration of the forehead and lower lip, compound fracture of the mandible and nose, fracture of the left humeral shaft. The patient was treated for shock. The abdominal wall was rigid on admission, a diagnosis of lacerated abdominal viscus and hemorrhage was made, and operation was performed when recovery from shock permitted. The blood pressure at that time was 130/100, pulse 116, temperature 99° F.

Operative Pathology.—Six to 700 cc. of beef broth-like fluid was present in the ab-

domen, and fat necrosis was noted in the right upper abdomen and great omentum. Examination of the pancreas and its entire extent, through the gastrocolic omentum revealed an apparently normal pancreas and an empty lesser sac. A perforation in the first portion of the duodenum, about the size of a pea, was found through which duodenal contents was escaping. There was no induration surrounding the perforation, and there was no evident effort being made to wall it off. Three layers of sutures, plus a tag of omentum, closed the perforation. Culture of the peritoneal fluid showed *Staphylococcus aureus*. The patient developed signs of peritonitis and pneumonia and died September 11, 1938, three days after operation.

Autopsy revealed general peritonitis and fat necrosis, wound infection, and a tight, sutured perforation of the first portion of the duodenum. The pancreas was apparently normal. Its ducts were not lacerated. There was bronchopneumonia. A microscopic examination of the pancreas revealed only the usual postmortem changes.

Discussion.—Dragstedt, Haymond and Ellis,¹ repeated the demonstrations of previous investigators, that inactivated pancreatic juice may be poured into the peritoneal cavity without immediate serious consequences. They also showed that sterile *succus entericus*, placed in the peritoneal cavity, is relatively innocuous. When, however, infection becomes a factor, peritonitis and fat necrosis cause rapid death.

These findings are probably an adequate explanation of the foregoing cases. In one, there was no gross pancreatic injury found at operation and, in the other, no gross or microscopic evidence of pancreatic injury found at autopsy.

Boyd² notes that acute, microscopic necrosis of the pancreas may occur without gross evidence of its presence. This, therefore, may have been the condition in the unautopsied case but not in the other.

Fat necrosis consists of a breaking down of fat by means of activated trypsinogen and lipase. The trypsinogen is activated by enterokinase derived either from the *succus entericus* or from the breaking down of traumatized cells. The activated trypsinogen must get under the peritoneal covering to get at the fat cells and kill them, permitting the lipase to break down the fat into fatty acids and glycerin. The peculiar spotty appearance of fat necrosis suggests lymphatic spread, and we know that this spread may at times penetrate the diaphragm and involve the pleura and pericardium.

One wonders why, if duodenal rupture be the cause of fat necrosis at times, one does not find the condition more often. Certainly the writer has never seen fat necrosis complicating the perforation of an ordinary duodenal ulcer, and questioning of others has not elicited it as having been a factor in this condition. Certainly, it is worthy of note that the finding of fat necrosis in a traumatic abdomen should direct one's attention to the first and third parts of the duodenum if no pancreatic injury appears after exploration of both peritoneal cavities.

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TOTAL CYSTECTOMY WITH BILATERAL NEPHROSTOMY FOR CARCINOMA OF THE BLADDER

FIVE-YEAR RESULT

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Case Report.—The patient, a male, age 51, was admitted to Mt. Sinai Hospital, in August, 1934, with the following history: He had had gross hematuria for five months for which he was treated with bladder lavages. When he came to the hospital his urine was grossly bloody; he urinated many times during the day and ten or 12 times at night. He had lost 40 lbs. of weight during the four months prior to entering the hospital. When admitted, he was in an emaciated, cachectic condition, running a temperature between 102° and 104° F. Roentgenologic examination of the kidneys was negative for calculi. Intravenous pyelography showed some dilatation of the right kidney with poor visualization, whereas the left kidney was apparently normal. Cystograms were then taken which showed a huge filling defect in the bladder, representing the tumor that was later removed. He was then cystoscoped, with difficulty, on account of the marked hematuria. This showed a tremendous neoplasm occupying the greater part of the bladder, extending down to the internal sphincter and covering over the trigonal region so that the ureteral orifices could not be visualized. A biopsy was taken from the tumor which was reported as an infiltrating squamous cell carcinoma with areas of necrosis. The patient was in such a debilitated condition nothing could be done for three or four days, except to give him several transfusions. He had no kidney tenderness, but we suspected that the temperature was probably due to infection of the right kidney. At that time his hemoglobin was 35 per cent, and he had received three transfusions.

On August 14, 1934, a right nephrostomy was performed. On opening the kidney there was escape of purulent urine. A tube was introduced through the cortex into the pelvis of the kidney. There was remarkable improvement following this nephrostomy. The temperature dropped to normal in 48 hours, and the general condition improved. He looked like a different individual. He was given small transfusions at short intervals so that, in about two weeks' time, he was in such good condition that we considered it advisable to go ahead with the second stage of the operation. After reviewing the cystograms and the cystoscopic picture we decided there was only one thing to do—total cystectomy. The tumor was too huge for radiation or partial resection; it was either do nothing at all or a total cystectomy. This was performed, August 24, 1934.

Operation.—Through a midline incision, an enormous bladder was exposed, which made mobilization rather difficult despite the long incision. After tying off the vesicular arteries, the bladder was mobilized down to the prostate. The bladder, seminal vesicles and half of the prostate were removed in one piece, without opening into the bladder. The left ureter was mobilized, cut across and implanted in the anterior abdominal wall just internal to the anterior superior spine. The patient did well for two days. Then the temperature rose to 102° F. He was draining well through the right nephrostomy wound; we noticed, however, that drainage had stopped from the left nephrostomy in the skin. We found that this ureter had retracted. In view of the nephrostomy on the right side, it was thought best to perform a nephrostomy on the left side instead of another reimplantation of this ureter. This was done, and the patient improved remarkably. The temperature dropped to normal, and he was discharged from the

hospital after five weeks. Within six months he had gained 40 lbs. in weight, his hemoglobin rose from 35 to 70 per cent, and he was in excellent condition.

Subsequent Course.—The patient has been followed to the present time. The post-operative treatment consisted in changing his nephrostomy tubes once every two weeks with occasional pelvic lavages. On-and-off, he has had some form of urinary antisepsis. He was well until 1936, when he was admitted for bleeding from the left nephrostomy tube. Roentgenologic examination showed no calculi. After a few pelvic lavages this stopped and he was discharged after a few days. He went along in very good condition until 1939, when he was readmitted because of trouble with the drainage through the right nephrostomy tube. Examination showed that there was a calculus in the nephrostomy sinus. This was easily removed after dilating the sinus, and he has been well ever since.

We feel that total cystectomy has a definite place in the management of certain types of bladder carcinoma, particularly extensive cancer, such as this was; in large tumors involving the neck of the bladder and the trigonal region; and those growths that, to a large extent, infiltrate from the bladder into the prostate. Our method of choice is total cystectomy with skin implantation preferably in two stages. At the first stage, both ureters are implanted in the skin, after which the bladder is removed. Most of these kidneys are infected, the ureters are generally dilated so that there is a large risk attached to performing an ureterosigmoid implantation. When dealing with non-infected kidneys and normal ureters, implantation into the sigmoid is perhaps the preferable procedure.

We have performed 27 total cystectomies to date, with an operative mortality of 22 per cent. The longest survival after an operation, such as this one, has been nine years, and this patient did not die of a metastatic lesion but of renal infection. We have patients who have survived cystectomy four, five, seven, and eight years. About 50 per cent of the patients who survived the operation have lived five years or longer.

ABSTRACTS OF PAPERS
PRESENTED BEFORE THE FIRST ANNUAL ASSEMBLY
OF
THE CENTRAL SURGICAL ASSOCIATION
ANN ARBOR, MICH., FEBRUARY 28—MARCH 2, 1941

CARCINOID TUMOR OF THE CECUM

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ONLY 11 CASES of carcinoid tumors of the colon have been reported, in five of which the lesion was in the cecum. Wyatt was able to collect reports of eight cases of carcinoid tumors of the large bowel from the literature, and reported one of his own. In three cases of this series the cecum was

tumor, cecum, and appendix were removed, and pathologic examination revealed adenocarcinoma, Grade I, of the so-called carcinoid type. The tumor measured 2 cm. in diameter, and was situated in the cecum at the base of the appendix, with obstruction of the appendiceal lumen (Figs. 1, 2 and 3). Ex-



FIG. 1.—Gross specimen: Showing cecum with tumor, and its relation to appendix.

involved. Besides these three, we wish to call attention to two more, and to report a sixth case, which makes the total number of carcinoid tumors of the colon, 12. The first was reported by C. W. Mayo, in 1933, and the second case has been reviewed in detail recently by Mayo and Wilson.

CASE REPORT.—The patient, a female, age 20, was operated upon for perforative appendicitis with peritonitis and, in addition, was found to have a small tumor in the cecum at the base of the appendix. The

amination of the appendix revealed acute purulent appendicitis.

COMMENT.—There are now six known cases of carcinoid tumor of the cecum. The clinical record in one is not available; in two, the tumors did not produce symptoms; in two, they caused symptoms of obstruction (one by intussusception, although it was situated at the appendoceleal junction); in the remaining case the tumor was located in the cecum near the base of the appendix, and caused acute obstructive appendicitis. In

only one of the six cases were the tumors multiple. In two, metastasis was demonstrable. In the case we have reported, no attempt was made to explore the general ab-

cially in the base at the crypts of Lieberkühn. They grow slowly, and their relative infrequency probably will continue to prevent their preoperative diagnosis. However, their



FIG. 2.—Showing relation on bisection.

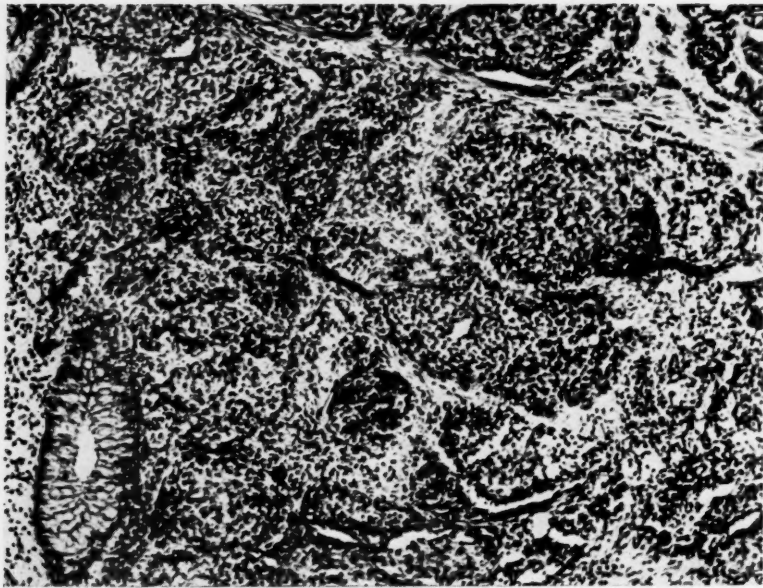


FIG. 3.—Photomicrograph showing pathologic characteristics of the carcinoid tumor. Grade I. ($\times 100$)

dominal cavity because of the peritonitis.

The tumors are thought to originate in the cells of Kulchitsky, which are found throughout the gastro-intestinal tract, espe-

cially in the base at the crypts of Lieberkühn. They grow slowly, and their relative infrequency probably will continue to prevent their preoperative diagnosis. However, their relative benignancy makes local excision feasible, and any extensive type of resection seldom necessary, unless their pathologic characteristics are questionable.

THE CLINICAL SIGNIFICANCE OF HUMAN GASTRIC MOTILITY*

Frank E. Hamilton, M.D.

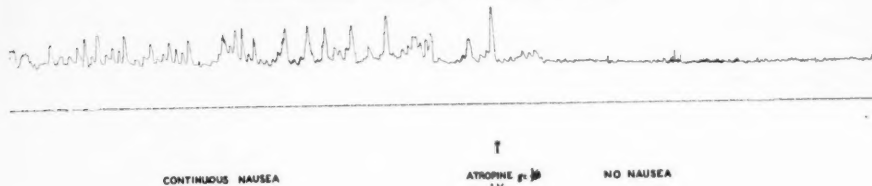
Columbus, Ohio

From the Department of Research Surgery, the Ohio State University, Columbus, Ohio

THE MOTOR ACTIVITY of the human stomach is of demonstrable clinical importance. It is affected not only by disturbances in gastric physiology, but also by certain pathologic changes occurring elsewhere in the gastro-intestinal tract. In earlier investigations of the department,^{1, 2, 3, 4, 5} the balloon and kymograph method was used to study the influence of the extrinsic innervation; the reaction of the stomach following celiotomy; and the effect of drugs upon gastric motility.

benign obstructive duodenal ulcer revealed kymographic evidence of gastric hyperactivity occurring simultaneously with clinical evidence of pylorospasm. Spontaneous hypomotility of the stomach was associated with simultaneous relief from pain. Activation of the stomach following administration of morphine or the atropine-prostigmine sequence was associated with epigastric pain. Following administration of atropine or ephedrine gastric quiescence ensued, and at once the pain ceased.

KH 11-10-1958
ESOPHAGO-PLEURAL FISTULA
NAUSEA SIX DAYS FOLLOWING APICAL THORACOPLASTY
BALLOON INTRODUCED INTO STOMACH THRU GASTROSTOMY STOMA



GRAPH 1.—The control of late postoperative nausea. Continuous nausea was observed throughout the period of gastric hypermotility. Coincident with the onset of gastric hypomotility there was complete relief from nausea.

With these studies as a background we are now investigating clinical variations in gastric motility. A patient who complained of postoperative "gas pains" was studied. The kymograph recorded greatly increased gastric activity coincident with clinical evidence of pain. Decreased gastric activity and simultaneous cessation of pain followed administration of atropine.

Late postoperative nausea was studied on a patient with a permanent gastrostomy. The balloon was inserted directly through the gastrostomy opening, and the stomach was found to be in constant, irregular hyperactivity. During this period the patient complained of continuous nausea. Following intravenous administration of atropine there was immediate cessation of gastric activity along with complete relief of the nausea (Graph 1).

Preoperative studies of a patient with a

The relation of gastric motility to biliary colic was investigated upon a patient who, at subsequent operation, was shown to have the gallbladder, cystic duct, and common duct filled with small cholesterol stones. Preoperatively, the patient had occasional attacks of upper right quadrant pain, clinically indistinguishable from biliary colic. A motility investigation during such an attack revealed constant gastric hyperactivity. Administration of intravenous atropine was quickly followed by gastric quiescence, and complete relief from pain. Morphine reversed the action of atropine and, coincident with the pronounced irregular gastric hyperactivity, the patient again complained of colic-like upper right quadrant pain indistinguishable from the pain of biliary colic (Graph 2).

From these studies it appears that gastric motility is affected by certain lesions of the

* We are indebted to Abbott Laboratories, Inc., for the intravenous preparations of atropine and morphine; also to Hoffman-LaRoche, Inc., for the prostigmine used in this investigation.

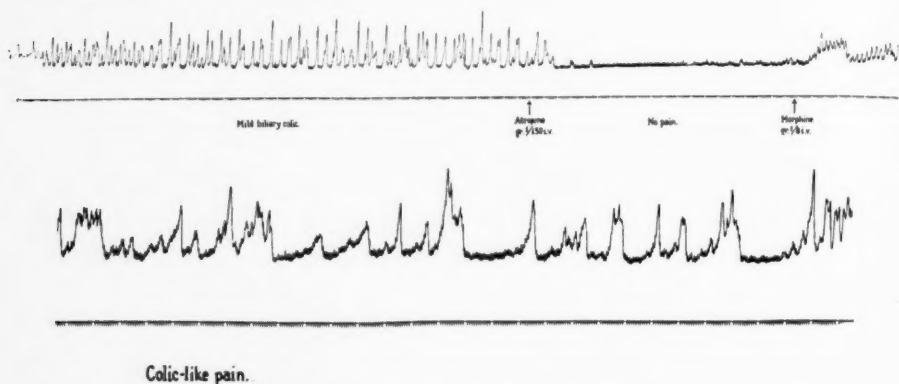
This investigation was aided by a grant from the Comly Fund for Research of the Ohio State University.

stomach as well as by certain lesions of more distal intestine similarly innervated. In the cases reported, clinical discomfort occurred simultaneously with kymographic evidence of gastric hypermotility, whether that hypermotility was spontaneous or induced by the administration of morphine or the atropine-prostigmine sequence. Conversely, the pa-

of Morphine and Atropine on the Human Stomach. *Jour. Pharm. and Exper. Therap.*, **61**, 230, 1937.

⁵ Veach, Harry O., Lauer, B. R., and James, A. G.: Effects of Prostigmine and Atropine on the Human Stomach. *Jour. Pharm. and Exper. Therap.*, **62**, 422, 1938.

N.K. 7-6-39 Stomach.
Control of Biliary Colic.



GRAPH 2.—The symptomatic control of biliary colic due to cholecystitis with cholelithiasis. Continuous upper right quadrant pain, indistinguishable from that of biliary colic, was noted throughout the entire period of gastric hypermotility. Complete clinical relief was noted coincident with gastric hypomotility induced by the intravenous administration of atropine. Morphine reversed the action of atropine and with the recurrence of gastric hyperactivity the patient again complained of severe pain indistinguishable from that of biliary colic.

tients ceased to complain of pain when the stomach was quiescent, whether that quiescence was spontaneous or was induced by the administration of atropine or ephedrine.

Abnormal motility of the human stomach would seem to be often associated with common abdominal disorders. Control of the abnormal gastric activity by means of standard drugs will often simultaneously control the clinical symptoms.

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DISCUSSION.—DR. J. C. SCHNEDORF (Kansas City): I should like to ask Doctor Hamilton whether he has differentiated the hypermotility in the different clinical conditions of the stomach from the hypermotility of the stomach as seen in hunger contractions, and whether he has tried controlled injections, such as injecting saline. That certainly has a sedative effect upon the hypermotility of the stomach.

DR. FRANK E. HAMILTON (Columbus, closing): There is very little similarity between hunger contractions and the gastric hypermotility associated with the type of gastro-intestinal disorders described in this paper. Moreover, although the gastric motility investigations are conducted under controlled conditions with an empty stomach, they are not continued until such a time as the patient complains of hunger. As a further control, whenever possible, we use intravenous drugs for immediacy of action, so that if a motility change is observed, it will have been clearly due to the drug action. Control injections, such as intravenous saline, have not altered gastric

motility if administered during a period of hypermotility due to pathologic lesions, such as biliary colic or pylorospasm.

DR. STUART C. CULLEN (Iowa City): I should like to ask Doctor Hamilton if he has used a combination of drugs simultaneously, such as morphine and atropine together?

DR. FRANK E. HAMILTON (Columbus,

closing): Yes, we have used morphine and atropine, together, in the usual preoperative dosage of 1/6 grain of morphine and 1/150 grain of atropine, or 1/4 grain morphine and 1/100 grain of atropine. Following such an injection, gastric hypermotility is observed. The hypermotility is, as a rule, less marked than when morphine is administered alone, but a definite period of gastric hypermotility usually follows the injection of morphine and atropine.



PERITONEAL FLUID IN PERFORATED PEPTIC ULCERS

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THERE IS fairly general agreement that intra-abdominal infection is the chief cause of death following perforation of a gastric or duodenal ulcer. This is borne out by a series of 98 individuals who have had simple closure of perforated ulcers at the Receiving Hospital during the past two years. Of these, ten died and eight were autopsied. Six died of severe, acute diffuse peritonitis and two had large intraperitoneal abscesses. The time interval between perforation and operation varied widely in this group, ranging from two to 48 hours.

Our observations on a number of patients who have had simple closure of perforated ulcers, have convinced us that chemical irritation of the peritoneum is of relatively little significance in influencing the general mortality as compared with bacterial contamination.

Swab cultures of the peritoneal fluid in 67 cases were productive of bacterial growth in 43 instances, and negative in 24. From 34 cases, both a swab and a larger specimen, usually 3 cc. were separately cultured in each case. This was done to determine if dilution might be responsible for some of the negative cultures. Twenty-seven of the 3 cc. specimens gave bacterial growth but only 19 of the swabs were positive.

More recently, colony counts have been made on agar plates inoculated with 3 cc. of peritoneal fluid. In the few cases studied there has been a general parallelism between the duration of the perforation, the volume of fluid, and the number of organisms per cubic centimeter.

The bacterial organisms most frequently recovered at operation have been in order of

frequency: *Streptococcus viridans*, non-hemolytic streptococci, staphylococci, and *B. coli*.

The assumption that bacterial growth is modified by gastric secretion implies that there is a high concentration of gastric hydrochloric acid at the time of perforation. Our results show that the hydrogen ion concentration of the gastric contents at the time of operation is low. The individual pH values varied widely ranging from two and one-half to eight, most being between pH four and eight. Furthermore, we have, in almost every case, obtained bacterial growth from the gastric contents at the time of operation.

The nature of the fluid in the peritoneal cavity was of interest to us because of its relation to bacterial growth. To our surprise, we found that, in almost every case, the peritoneal fluid was neutral, with a pH very close to seven. The chloride content of each specimen was uniformly that of blood plasma. The plasma-like character of the peritoneal fluid was constant, regardless of the duration of the perforation or the volume of fluid in the peritoneal cavity.

In summary, we find that micro-organisms are present in the peritoneal cavity very shortly after ulcer perforation. The gastric acidity is low at the time of operation, and bacteria are to be found in the gastric contents. The peritoneal fluid at operation has an hydrogen ion concentration and chloride content approaching blood plasma. Thus, we find no evidence which would indicate modification of the activity of bacterial growth by gastric contents or by peritoneal fluid.

CIRCULATION OF THE SMALL INTESTINE

A Comparison of Man with Laboratory Animals

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DETAILED STUDIES of the distribution of the superior mesenteric vessels and their branches have been made in the following animals: Man, dog, cat, rabbit, opossum, raccoon, and a species of kangaroo. The vessels have been injected with liquid latex, and the specimens then fixed and cleared by a modification of the Spalteholz technic. These preparations clearly demonstrate differences in the intestinal blood supply of

dog and man, differences so great as to make the dog inadvisable to use as an experimental animal for studies on the effect of distention on the blood supply of the human intestine. Some of the other species show a greater resemblance, but the search is being continued in an effort to find a laboratory animal more comparable to man in this respect, in order that experimental data may be better evaluated.



NERVE COMPRESSION SYNDROME AND SURGERY FOR A CERTAIN TYPE OF SCIATIC NEURITIS

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THE CHIEF PURPOSE in presenting this paper is to call attention to a certain group of patients who have suffered for at least a number of months from a sciatic neuritis, which in our experience has been found to be due not to a ruptured intervertebral disk or to hypertrophied ligamenta subflava, but rather to encroachment upon the nerve or nerves by one or several of the other anatomic structures adjacent to the intervertebral foramina.

We have reviewed 42 consecutive cases upon whom laminectomies were performed and who have been followed for a period of from six months to three years after operation. For this paper we have focused our attention on (1) the type of lesion found; (2) the extent of exploration which was performed; and (3) the end-results.

In this group, we found only 25 per cent due to ruptured intervertebral disks, and in only 7 per cent was the etiologic factor apparently thickened ligamenta subflava. In the remaining 68 per cent, we found the compressing or irritating factor to be one or several of the following structures: (1) A narrowed intervertebral foramen; (2)

a prominent but not ruptured intervertebral disk or hypertrophic arthritis; (3) abnormally dilated lumbar veins accompanying the nerves into the foramina; and (4) adhesions to a nerve from previous inflammation or subarachnoid alcohol injection. The important feature seemed to be the combination of two or three of the encroaching factors, as without this there might have been chances for compensatory relief from the pressure or irritation. To designate this group of cases, we have been using the term "Nerve Compression Syndrome."

In our experience, this latter group of cases has differed from those due to ruptured intervertebral disks, in that the history of trauma has been less definite and the roentgenologic evidence with air or lipiodol has been less clear-cut. The history of persisting incapacitating pain, the objective evidences of sciatic neuritis, and the changes in the total protein of the spinal fluid have been about the same in the two groups.

The extent of operative exposure that was necessary depended upon the findings. With a localized protruded portion of ruptured disk, a limited exposure usually suf-

RETROPERITONEAL HEMORRHAGE

ficed. But if this was not found, we continued exposure of the nerves involved, until we were certain that all possible compressing factors were removed, even including removal of overhanging borders of facets at the foramina. In our experience thus far, it seems that the end-results were better where this more extensive exposure was made.

The end-results in this group thus far have been very satisfactory as judged by the patients' own estimate of percentage of relief of symptoms. Thus far, the only poor results were with ruptured disks and of

these, two were definitely psychoneuroses associated with compensation.

In summary, we wish to call attention to a group of patients with sciatic neuritis which seems to be due to a combination of pressure and irritative factors other than protruded intervertebral disks and hypertrophied ligamenta subflava.

We propose the term "Nerve Compression Syndrome" for this miscellaneous group. We advocate adequate surgical removal of all or sufficient compressing factors. More time must pass before we can evaluate with certainty the final end-results.



RETROPERITONEAL HEMORRHAGE

With Special Reference to the Accompanying Paralytic Ileus

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RETROPERITONEAL HEMORRHAGE may be due to traumatic and nontraumatic factors. It is invariably associated with a paralytic ileus. Among the more common traumatic factors are direct injury to retroperitoneal tissues, fractures, and operative trauma. Of the nontraumatic causes rupture of an abdominal aorta and spontaneous perirenal hematomata were most frequently encountered.

Several unusual cases of retroperitoneal hemorrhage were observed at the Evanston Hospital. The first case was a retroperitoneal hemorrhage following an appendicectomy. The source of the hemorrhage was the lateral ascending branch of the deep circumflex artery. This vessel is frequently encountered and often traumatized in the course of an appendicectomy through a McBurney's incision. Ligation of this vessel is advised.

The second case was a retroperitoneal hemorrhage into the broad ligament following a vaginal hysterectomy. Recovery occurred in both cases but only after stormy postoperative courses due to paralytic ileus.

Seven cases are reported of patients who died of ruptured abdominal aorta retroperitoneally. The clinical findings in these patients were quite similar to those of retroperitoneal hemorrhage from other causes. The syndrome often simulates a

peritonitis. Severe abdominal pain followed by circulatory collapse, marked pallor, and often a palpable mass with abdominal rigidity are early findings. Later, within 24 hours to five days after onset of pain, a paralytic ileus develops. Roentgenogram of the abdomen reveals the aneurysm in 75 per cent of abdominal aneurysms.

Patients with perirenal hematomata had renal pain, signs of hemorrhage, and a palpable tumor.

Treatment of the retroperitoneal hemorrhage depends upon the cause. Prognosis was better in the traumatic group.

Paralytic ileus was found frequently following a retroperitoneal hemorrhage. The mechanism of the reflex seemed to be due to a paralysis of the splanchnic and parasympathetic systems, and not a stimulation of the splanchnic system alone.

Whatever the explanation of the physiologic processes involved may be, the condition is quite serious. Wangenstein suction and occasionally enterostomy have been necessary for relief of the ileus. Evacuation of the hematoma only, in those conditions which allowed this procedure, is recommended. Ligation of the abdominal aorta for aortic aneurysm before hemorrhage occurs should be attempted in selected cases. In any case the prognosis should be guarded.

THE PATHOGENICITY OF THE BACTERIA OF APPENDICITIS
PERITONITISWilliam A. Altemeier, M.D.
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PERITONITIS secondary to acute perforated appendicitis is rarely caused by a single type of bacterium. On the contrary, the bacterial flora of the peritonitis exudate is mixed and varied, and any of the intestinal bacteria, either aerobic or anaerobic, may be found.¹

In this communication, the pathogenicity of these bacteria for experimental animals has been studied. The majority of the aerobic strains tested produced minor local lesions or cellulitis when injected subcutaneously, but their intraperitoneal injection usually failed to cause a fatal peritonitis. The aerobes capable of producing a fatal peritonitis included some strains of *B. coli*, *B. pyocyaneus*, and *B. alkaligenes*. Twenty-one strains of *B. coli* were thus tested, and three of these were quite virulent, producing large areas of cellulitis and rapidly fatal peritonitis. The remaining 18 produced minor local subcutaneous lesions, but no fatal peritonitis.

The virulence of the aerobic bacteria, particularly *B. coli*, for guinea-pigs and rabbits, could be greatly increased by the coincidental intraperitoneal injection of many particles of autoclaved sterile tissue through a large-bore needle. Similar observations had been made by Halsted,² working with the *Staphylococcus*.

Many of the anaerobic organisms were difficult to cultivate in pure culture. By using deep tubes containing brain broth and a small amount of blood, a fairly good growth was usually obtained under strict anaerobic conditions. The majority of the anaerobic bacteria investigated did not produce a fatal peritonitis, with the exception of hemolytic streptococci, *B. thetoides*, and *B. fragilis*. The *B. melaninogenicum*, frequently found in our series¹ of peritonic exudates, was very difficult to separate from an anaerobic *Streptococcus*, with which it was frequently and intimately associated. It was found to be relatively nonpathogenic.

If several or more species of these bacteria, found in a given case of peritonitis, were mixed and cultivated, simulating their ex-

istence in the peritoneal exudate, their composite virulence was greatly increased. Equal, or smaller doses of the mixed cultures usually produced extensive areas of cellulitis with gangrene and overwhelmingly fatal peritonitis. The synergistic effect produced by these groups of bacteria was repeatedly demonstrated.

Symbiosis in disease has attracted relatively little attention in medicine and surgery. The fulfillment of Koch's postulates by a single species of bacteria is generally required for the establishment of the etiology of disease. In discussing the rôle of *C. welchii* in appendicitis, Jennings,³ in 1923, believed that *C. welchii* infection occurred, as a rule, in symbiosis with a number of other bacteria. The experiments of Weinberg, Prevot, Davesne, and Renard,⁴ in 1928, suggested the possibility that not only appendicitis but also peritonitis was the result of the combined action of bacterial mixtures. After studying the pathogenicity of *B. coli*, nonhemolytic streptococci, and *C. welchii* in pure and mixed culture, Meleney, Olpp, Harvey and Jenn⁵ clearly demonstrated the synergistic activity of these three symbionts in peritonitis. In our experiments, these findings have been substantiated, and a similar accumulative action of many more species of aerobic and anaerobic bacteria has been shown. These experiments give credence to the previous observations that the clinical course of the illness was much more serious if more than one type of intestinal bacterium was present in the peritoneal exudate than if only one was present.

In summary, an analysis of the literature, and our experiments indicates that appendicitis peritonitis is usually a "polymicrobial" infection caused by the synergistic pathogenic action of a group of bacteria existing in a state of symbiosis. Correlation of clinical and experimental studies shows that, in general, the greater the number of intestinal bacterial species present in the exudate, the greater the severity of the peritoneal infection is likely to be.

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DISCUSSION.—DR. ROY MCCLURE: I should like to ask Doctor Altemeier whether he has done any work in connection with sulfanilamide or its derivatives, and whether it has any specific action with this group of bacteria that he has shown us.

DR. W. A. ALTEMEIER (Cincinnati, closing): I have not done much work with the sulfonamides in relation to peritonitis except on a group of rabbits in which I injected lethal amounts of similar mixed cultures to those shown on the slides. If I injected sulfanilamide coincidentally with the mixed cultures, the animals were saved in a large percentage of the cases—some 75 per cent, as I remember. If the injection of the sulfanilamide was delayed as long as four hours after this particular mixed culture was injected, the animals never survived. In the control animals, 100 per cent of the animals would die after the injection. So the evidence that I had pointed to the fact that in rabbits, sulfanilamide, if administered at the time of the injection or shortly after, protected the animals in a large percentage of the cases; if delayed, it failed to protect them.



TISSUE REACTIONS TO SUTURE MATERIALS

A Preliminary Report

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METHODS OF STUDY.—A series of experiments have been carried out utilizing the anterior chamber of the rabbit's eye in an effort to standardize the effects of trauma, tension, and hemostasis. The fact that the anterior chamber of the eye is an excellent culture medium is apparent from the ease with which tissue cultures and experimental neoplasms may be grown in this site. Small segments of suture material placed in the anterior chamber may be observed grossly through the transparent cornea, and cell counts made of the aqueous humor at varying intervals may be taken as a quantitative index of the reaction. One centimeter segments of catgut, silk, stainless steel wire, nylon, silkworm catgut, and ordinary spool cotton have been placed in the anterior chamber under aseptic technic.

In an effort to determine whether catgut might possess antigenic propensities, another series of animals have been sensitized to

sheep serum, and catgut introduced into the eye subsequently. Employing the usual hemacytometer, cell counts have been made at varying intervals and cultures of the aqueous humor taken.

Results.—The marked difference in the reaction between the absorbable and non-absorbable sutures is strikingly apparent when this method of study is employed. In general, the reaction to silk is very minimal. For the first seven days there is practically no reaction and by the fourteenth day counts on the fluid have averaged 250 leukocytes per cubic millimeter. The reaction to ordinary spool cotton is similar. However, it has been noted that the cotton has less of a tendency to untwist. Although, perhaps not significant, the cell counts have averaged somewhat less. In certain animals, these sutures have been allowed to remain for the period of one year with no apparent harm to the eye whatever. The reaction to stain-

less steel wire can scarcely be measured. The vision of the eye is not impaired and cell counts made on the aqueous humor have averaged from five to ten leukocytes per cubic millimeter. However, when catgut is placed in the eye the aqueous humor becomes completely opaque in about ten days and the animal loses its vision completely. From outward appearances the anterior chamber is filled with pus. Cell counts of this fluid vary from 2,000 to 6,000 leukocytes per cubic millimeter. Cultures, in every instance, both in blood agar and beef broth have been negative.

In the group of animals in which sensitization to sheep serum has been carried out, precipitin studies have demonstrated the precipitins in concentrations from 1 to 50,000. One-tenth of a cubic centimeter of sheep serum subsequently introduced into the eye gives a marked inflammatory reaction, characterized by edema and the coagulation of exudate in the chamber in a very few hours. Likewise, segments of catgut placed in the eye of a sensitized animal produce a similar

severe reaction which has been interpreted as the Arthus phenomenon. The nonabsorbable sutures such as silkworm catgut do not produce this reaction in sensitized animals. Reaction to plain catgut is estimated to be twice as great as to chromic catgut. Likewise, the Arthus phenomenon produced with plain catgut, grossly, is more severe than that from chromic catgut.

SUMMARY

Preliminary studies indicate that the anterior chamber of the eye is a suitable medium for observing the reaction of tissue to suture material. Sutures may be introduced with a minimum of trauma; standard conditions are provided; gross observation may be made continuously; and quantitative cell counts may be made on the aqueous humor. A most striking difference in reaction is observed when nonabsorbable sutures are compared with catgut. Catgut apparently possesses antigenic propensities, inasmuch as the Arthus phenomenon has been produced in animals sensitized to sheep serum.

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